Generation and Succeeding Reactions of Allenyl Isothiocyanates

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In der vorliegenden Arbeit sind die [3,3]-sigmatrope Umlagerung von verschiedenen Propargylthiocyanaten und die doppelte [3,3]-sigmatrope Umlagerung von Eninylisothiocyanaten entweder durch Blitzvakuumthermolyse oder Thermolyse in Lösung untersucht worden.

Zusätzlich wurden die intramolekularen Reaktionen der resultierten Allenylisothiocyanate studiert. Außerdem sind die Reaktionsmechanismen zur Bildung der Thermolyseprodukte wie z.B. die [1,5]-sigmatropen Umlagerungen und die elektrocyclischen Ringschlüsse erklärt.

Die hochreaktiven Allenylisothiocyanate sind als geeignet elektrophile Vorläufer zur Synthese von neuen Thiazolen verwendbar, die an der C-2 Position substituiert sind. Dabei kommen verschiedene Nucleophile zum Ansatz. Für die Bildung dieser substituierten Thiazole sind die Regioselektivität, Stereoselektivität, Reaktionsmechanismen und der Bereich der einsetzbaren Nucleophile untersucht worden.

Stichworte: Isothiocyanat [= Senföle], Thiocyanat, Propargylthiocyanat, Allenylisothiocyanat, Eninylisothiocyanat, Thiazol, [3,3]-sigmatrope Umlagerung, [1,5]-sigmatrope Verschiebung, elektrocyclische Ringschlussreaktion, Heterocyclen.

Abstract

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PhD Thesis 2005, 127 Pages, 130 References, 12 Figures, 9 Tables, and 49 Schemes.

In this work, the [3,3] sigmatropic rearrangement of different substituted propargyl thiocyanates and double [3,3] sigmatropic rearrangement of enynyl isothiocyanates either by flash vacuum pyrolysis or by thermolysis in solution are studied.

Additionally, the intramolecular reactions of the resulting allenyl isothiocyanates are studied, and the reaction mechanisms for the generation of the final products, such as [1,5] sigmatropic migrations or electrocyclic ring closures, are explained.

These highly reactive allenyl isothiocyanates are used as appropriate electrophilic precursors for the preparation of novel examples of thiazoles substituted at C-2 position using different types of nucleophiles. For the formation of these substituted thiazoles, the necessary nucleophilicity as well as the regioselectivity, the stereoselectivity, and the reaction mechanisms are investigated.

Keyword: Isothiocyanate [= Mustard oil], Thiocyanate, Propargyl Thiocyanate, Allenyl Isothiocyanate, Enynyl Isothiocyanate, Thiazole, [3,3] Sigmatropic Rearrangement, [1,5] Sigmatropic Migration, Electrocyclic Ring Closure, Heterocycles.

In The Memory of My Beloved Mother

There are many devices in a man's heart; nevertheless the counsel of the Lord, that shall stand. *PROVERBS 19: 21*

Acknowledgement

The experimental part of this research was performed from October 2002 until December 2004 in the laboratories of Prof. Dr. K. Banert, Chemnitz University of Technology.

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My love and appreciation go also, to my father, sisters' families, and brother in Jordan for their continued support and love.

Finally, I deeply appreciate the Chemnitz University of Technology that embraced me as one of its students.

List of Symbols and Abbreviations

δ	Chemical shift
br	Broad
Cy	Cyclohexyl
d	Doublet
dd	Doublet of doublet
ddd	Doublet of doublet of doublet
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
dt	Doublet of triplet
ESI	Electron Spray Ionization
Et	Ethyl
Et_2O	Diethyl ether
EtOH	Ethanol
FVP	Flash Vacuum Pyrolysis
g	Gram(s)
°C	Grade Celsius
h	Hour(s)
Hz	Hertz
IR	Infrared
ITC	Isothiocyanate
ITCs	Isothiocyanates
J	Coupling constant
m	Multiplet
Me	Methyl
MHz	Mega Hertz
ml	Milliliter
m.p.	Melting Point
$[M^+]$	Molecule Ion
MS	Mass Spectrometer
m/z	Mass/Charge

min	Minute(s)
MeOH	Methanol
mmol	Millimol
NMR	Nuclear Magnetic Resonance
NOE	Nuclear Overhauser Effect
n-BuLi	*n*-Butyllithium
Ph	Phenyl
Ph_i	Ipso position of phenyl
Ph_m	Meta position of phenyl
Ph_o	Ortho position of phenyl
Ph_p	Para position of phenyl
q	Quartet
qt	Quartet of triplet
Roman numbers	Table of contents, General procedure numbers, and Summary
s	Singlet
sept.d	Septet of doublet
t	Triplet
t-BuOK	Potassium-*tert*-butanolate
THF	Tetrahydrofuran
THP	Tetrahydropyran
Ts	Tosyl
TsOH	Toluene-4-sulfonic acid monohydrate
wk	Weak

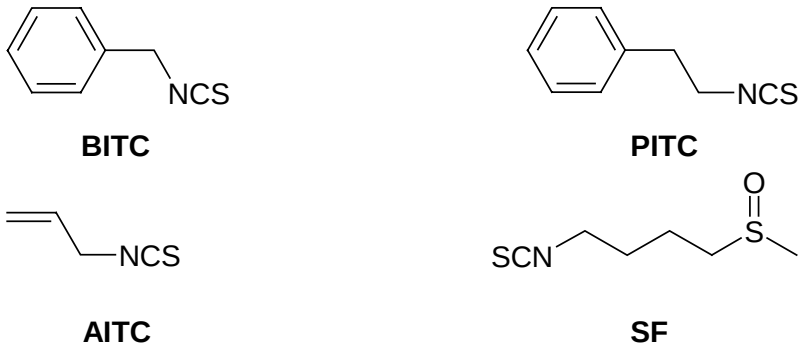
1 Introduction and Task of Study

1.1 Isothiocyanates

Isothiocyanates (ITCs) are a family of small organic compounds that occur in a wide variety of plants, many of which are consumed by humans on a regular basis.[1] However, they are also synthetically accessible.

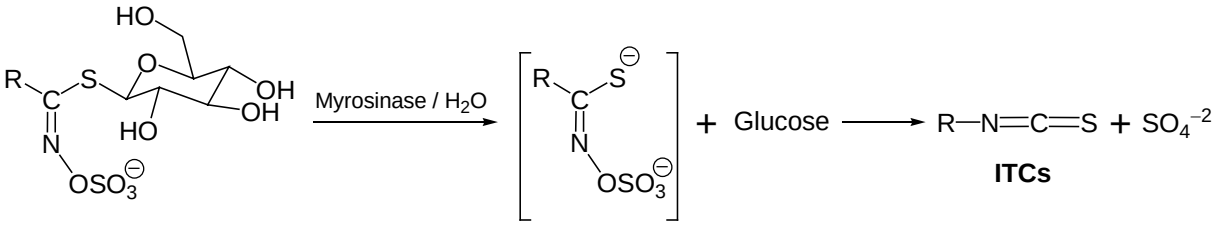
Over 20 natural and synthetic ITCs have demonstrated cancer preventive properties in animals treated with chemical carcinogens due to their inhibition of carcinogen metabolic activation. Moreover, several recent studies have suggested that humans who consumed higher level of ITCs might be less likely to develop lung and colon cancer.

Cruciferous vegetables (e.g. broccoli, kale, brussels sprouts, cabbage, mustard, garden cress, cauliflower, and water cress) are rich sources of benzyl-ITC (**BITC**), phenethyl-ITC (**PITC**), allyl-ITC (**AITC**), and sulforaphane (**SF**), see Scheme 1.



Scheme 1

Natural ITCs are products of degradation of glucosinolate precursors in cruciferous vegetables. When vegetables are chewed or chopped, the glucosinolates are cleaved by enzyme myrosinase to form **ITCs** (Scheme 2).



Scheme 2

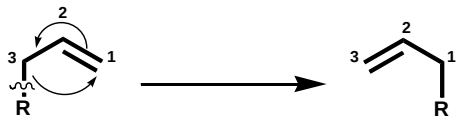
Finally, synthetic ITCs can be generated by different methods. Some of these methods are:

- Reaction of primary amines with sulfur compounds (e.g. thiophosgene[2a] or carbon disulfide[2b]),
- Addition[2c] of sodium azide, triphenylphosphine, and carbon disulfide to primary alkyl halides,
- Thermal isomerization[2d] of alkyl thiocyanates into alkyl ITCs,
- [3,3] Sigmatropic rearrangement[3-5] of allyl thiocyanates into allyl ITCs.

In this work, ITCs were mainly generated via a [3,3] sigmatropic rearrangement.

1.2 Sigmatropic Rearrangement

Sigmatropic rearrangement is a molecular rearrangement that involves both the creation of a new σ-bond between atoms previously not directly linked and the breaking of an existing σ-bond. There is normally a concurrent relocation of π-bonds in the molecule concerned, but the total number of π- and σ- bonds does not change (Scheme 3).[6]



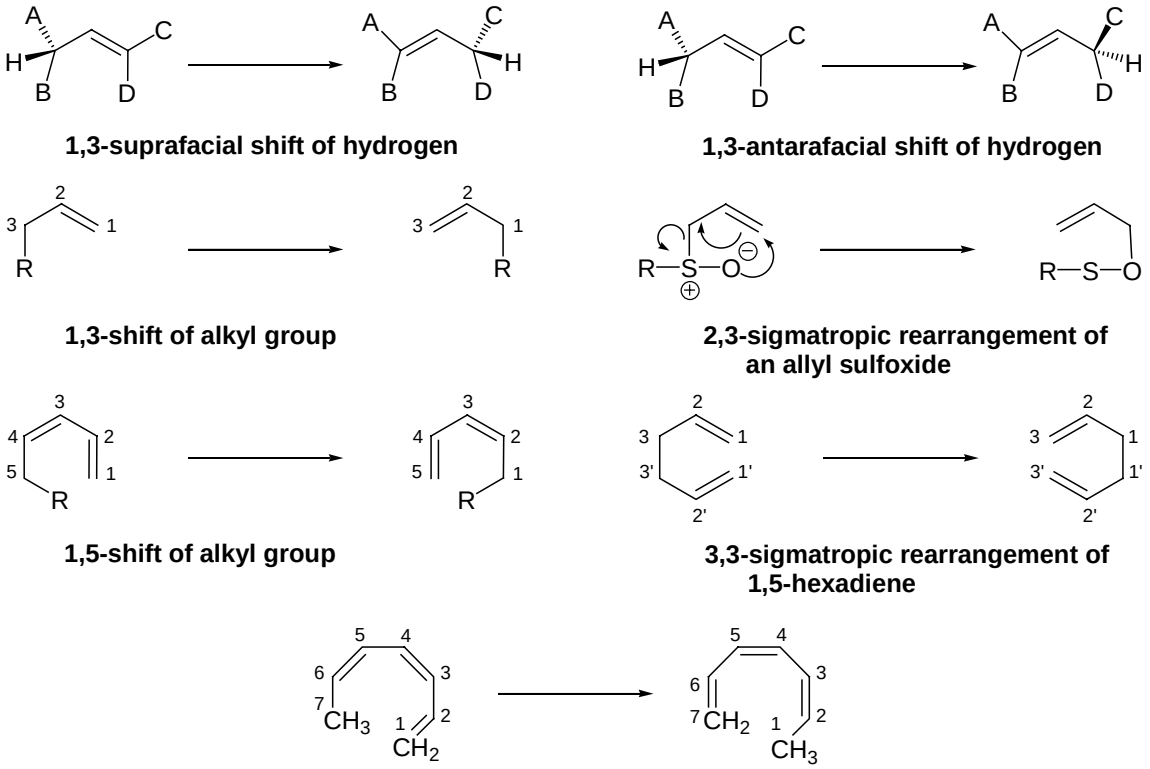
1,3-shift of alkyl group

Scheme 3

The relationship between the reacting centers in the migrating fragment and the π system (within the sigmatropic rearrangement) can be described by the order [*i*,*j*], where *i* is the

number of atoms in the migrating fragment and *j* is the number of atoms in the π system that are directly involved in the bonding changes. Some examples are shown in Scheme 4.

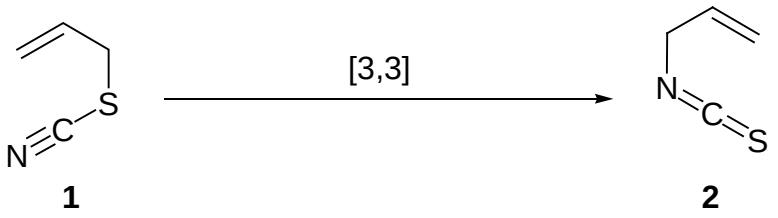
Indeed there are two topologically clear processes by which a sigmatropic migration can occur. If the migrating group remains associated with the same face of the conjugated *π* system throughout the process, the migration is called *suprafacial*. The alternative mode involves a process in which the migrating group moves to the opposite face of the *π* system during the course of the migration and is termed *antarafacial*.



Scheme 4

1.2.1 [3,3] Sigmatropic Rearrangement of Thiocyanates: Generation of Isothiocyanates

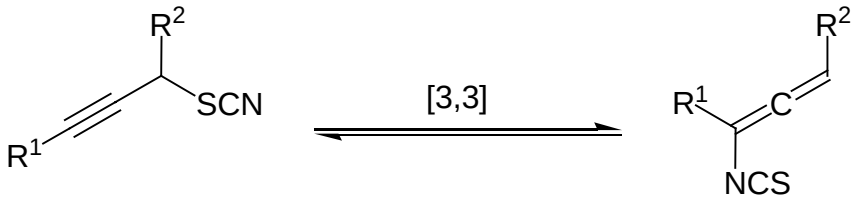
The isomerization of allyl thiocyanate **1** to allyl isothiocyanate **2** is a very old reaction,[3] which was discovered by Otto Billeter[4a] as well as by Gustav Gerlich.[4b] This type of isomerization is known as [3,3] sigmatropic rearrangement (Scheme 5).[5]



1 **2**

Scheme 5

Many attempts were carried out to prepare the isothiocyanates **4** by heating of thiocyanates **3** (Scheme 6), but resulted in only decomposed and polymerized products.[7]



3 **4**

Scheme 6

Nevertheless, Banert et al.[8] used an efficient method for the isomerization of propargyl thiocyanates **3** to allenyl isothiocyanates **4**, which was flash vacuum pyrolysis (FVP, flow thermolysis at high temperature and reduced pressure, Table 1).

Table 1

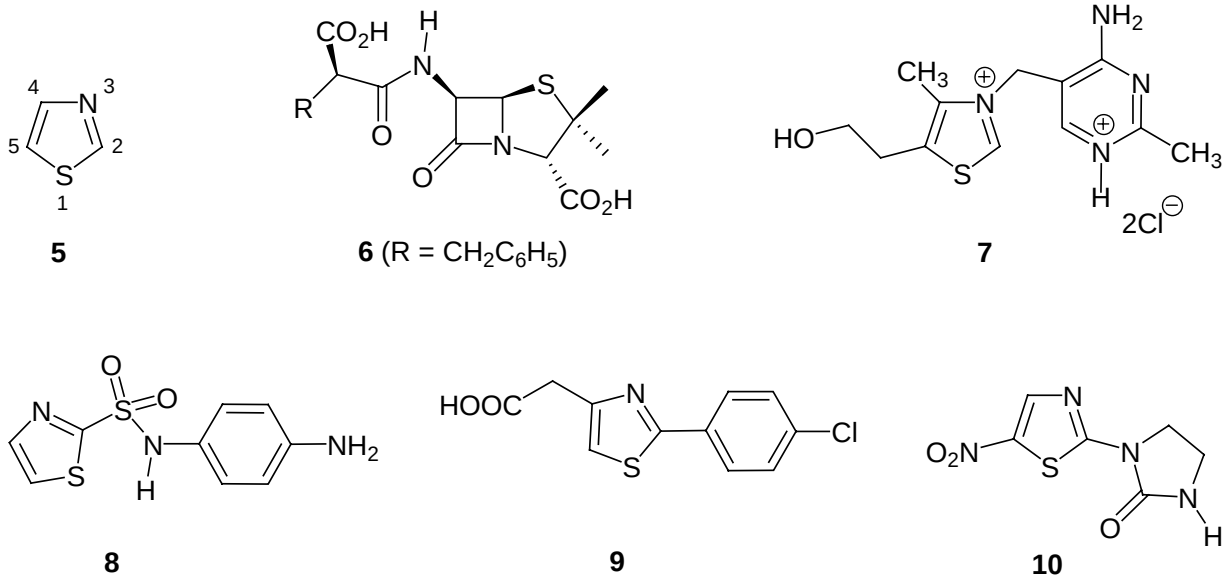
3/4	R^1	R^2	Conversion (%) of 3	Yield (%) of 4[a]
a	H	H	98	97
b	H	Me	≥99	97
c	Me	H	83[b]	ca. 100
d	CH_2Cl	H	≥96	60
e	$SiMe_3$	H	11[b]	ca. 100

[a]Isolated yield of **4** based on converted **3**. – [b]Under the conditions of flash vacuum thermolysis equilibria with **3c**/**4c** = 17:83 and **3e**/**4e** = 89:11 were established.

The equilibrium of **3** and **4** was established on FVP of **3c** and **3e** as well as renewed thermal reaction of the products **4c** and **4e**, which were separated by liquid chromatography. In the case of **4d** the yield was diminished since the precursor **3d** could not be vaporized without decomposition.

Although the isolated allenyl isothiocyanates **4a**,**b**,**d** were reactive and unstable, they were able to be reacted or trapped with different nucleophiles to form substituted 1,3-thiazole moieties.

The 1,3-thiazole unit **5** exists in many important naturally occurring compounds like penicillin **6** and thiamine (vitamin B1) **7** (Scheme 7).[9] In addition to **6**, many other thiazoles substituted at C-2 position exhibit pharmacological activities like sulfathiazole **8** (as antibiotic), 2-(4-chlorophenyl) thiazol-4-yl acetic acid **9** (as anti-inflammatory), and niridazole **10** (as schistosomicidal).[9]



Scheme 7

It is worthy to mention that the first 1,3-thiazole **5** was prepared by Hantzsch et al. via a reaction between thiourea and α-halo carbonyl compounds.[10]

Consequently, Banert et al.[8,11] reported the preparation of thiazoles **11** substituted at C-2 position via reaction of allene **4a**[8b] with different oxygen-, carbon-, nitrogen-, and sulfur-containing nucleophiles (Scheme 8). Although the allene **4a** was very reactive and was easily polymerized, the yield ranked between modest and good.

This method, an easy to deal with one-pot reaction, is efficient and the products can be easily separated.

4a **11**

Nu = *i*-Pr 91%

Nu = NHPh 82%

Nu = $SCHMe_2$ 70%

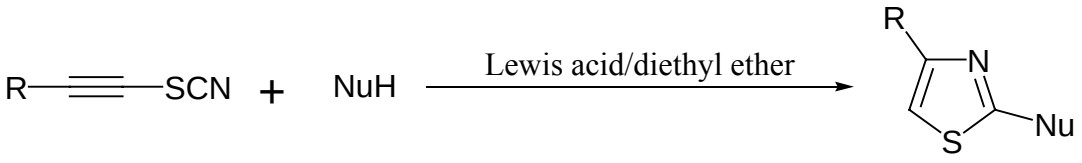
Scheme 8

1.3 Preparation of Substituted Thiazoles

Some other methods for preparation of thiazoles substituted at C-2 position are mentioned below.

1.3.1 From Alk-1-ynyl Thiocyanates

2,4-Disubstitued thiazoles **13** are prepared via the reaction of alk-1-ynyl thiocyanates **12** with different nucleophiles (NuH) like alcohols, phenols, secondary aliphatic amines, or thiols in the presence of Lewis acids (Scheme 9).[12]



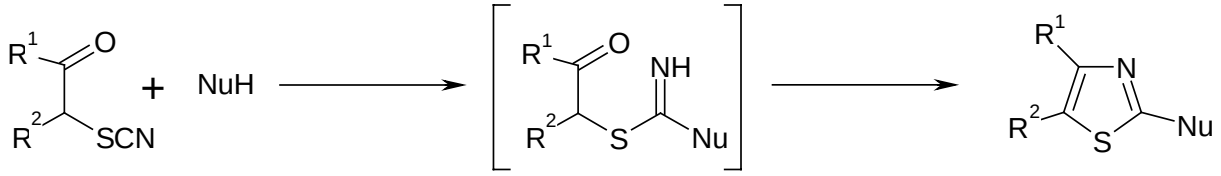
12 **13**

R = Ph, Nu = OMe	**70%**
R = Me, Nu = OPh	**79%**
R = Et, Nu = NEt_2	**70%**
R = *t*-Bu, Nu = SMe	**70%**

Scheme 9

1.3.2 From α-Thiocyanato Ketones

2-Substituted thiazoles **16** can be generated through the reaction of α-thiocyanato ketones **14** with different nucleophilic reagents (NuH) like water,[13] amines,[14-16] and C-nucleophiles[17] (Scheme 10). These reactions normally undergo via intermediates of type **15**.[13–17]



14 **15** **16**

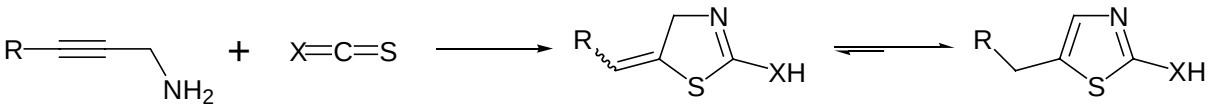
R^1, R^2 = –$(CH_2)_4$–, Nu = OH	**30%**	Ref. [13]
R^1 = Me, R^2 = Me, Nu = NHMe	**77%**	Ref. [16]
R^1 = Ph, R^2 = H, Nu = $CHCNCO_2Me$	**93%**	Ref. [17]

Scheme 10

1.3.3 From Alk-2-ynylamines and Isothiocyanates or Carbon Disulfide

5-Alkylidene-4,5-dihydrothiazoles **18** can be synthesized from reaction of different prop-2-ynylamines **17** with isothiocyanates[18] or carbon disulfide[19] (Scheme 11).

In some cases compounds **18** undergo isomerization to give 5-alkylthiazoles **19**.[18]



17 **18** **19**

R = H, X = S 88%

R = CH_2NEt_2, X = NCy 70%

Scheme 11

1.4 The Flash Vacuum Pyrolysis (FVP) Technique

The thermal transformation of allenyl isothiocyanates from propargyl thiocyanates proceeds efficiently by using the FVP technique. This process is also called gas-phase thermolysis. The main idea of this technique is to transfer the substrate into gas phase, under reduced pressure, through a long glass tube (about 45×1.5 cm filled with Raschig rings 3×3 or 4×4 mm) inserted horizontally in an electrical oven at high temperature. The product can be trapped in a bath cooled with liquid nitrogen (Figure 1). For the volatile starting materials a normal oil pump (final vacuum 10^{-3} Torr) can be used, while for the less volatile substrates an oil diffusion pump (final vacuum at least 10^{-5} Torr) must be used.

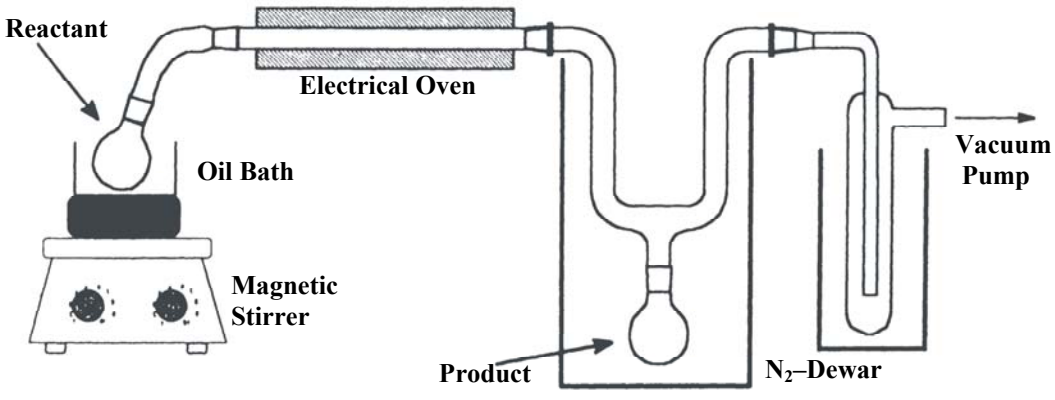


Figure 1

1.5 Task of the Study

In this study, the [3,3] sigmatropic rearrangement of different substituted propargyl thiocyanates and double [3,3] sigmatropic rearrangement of enynyl ITCs should be investigated either by FVP or by thermolysis in solution.

Additionally, the succeeding reactions of the resulting allenyl ITCs like 1,5 sigmatropic migration or electrocyclic ring closure, and synthesis of new substituted thiazoles have to be studied. Moreover, the reaction mechanisms (for most cases) should be explained for both the rearrangement of thermolized compounds and thiazoles formation.

These allenyl ITCs of type **4a**[8,11] have to be used as appropriate electrophilic precursors for preparation of substituted thiazoles of the type **11** (substituted at C-2 position) using oxygen-, nitrogen-, carbon-, and sulfur-containing nucleophiles.

Thus, the well-known allenyl ITC **4a**[8b] in addition to the newly prepared ITCs **21**, **25**, and **38** should be used as precursors for the preparation of thiazoles newly substituted at C-2 position.

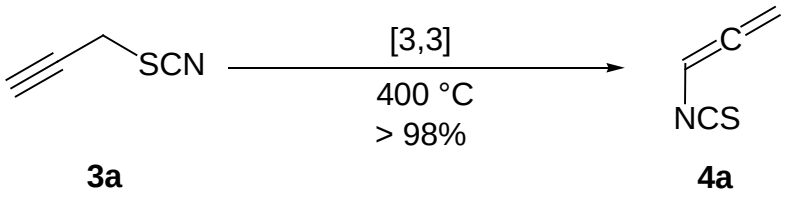
In these preparations, completely new systems of different types of nucleophiles have to be used not only to synthesize novel families of substituted thiazoles, but also to investigate the necessary nucleophilicity as well as the regioselectivity, the stereoselectivity, and the reaction mechanisms of the transformations.

2 Results and Discussion

2.1 Synthesis of Allenyl ITCs

2.1.1 Basic System of Allenyl ITC 4a

The allenyl ITC **4a** was efficiently prepared by K. Banert et al.[8b] via the [3,3]-sigmatropic rearrangement (Scheme 12). The equilibrium ratio between the propargyl thiocyanate **3a** and allenyl ITC **4a** was ranged between **3a**/**4a** 5:95 and 1:99, and the overall yield was >98%. ITC **4a** was obtained at 400 °C and 0.01 Torr, it was very reactive and could easily polymerize at room temperature. Therefore, the product was collected in an inert solvent as a 10% solution to hold down the polymerization process. It was found that allene **4a** is stable in solution (10%) for several weeks at –18 °C.



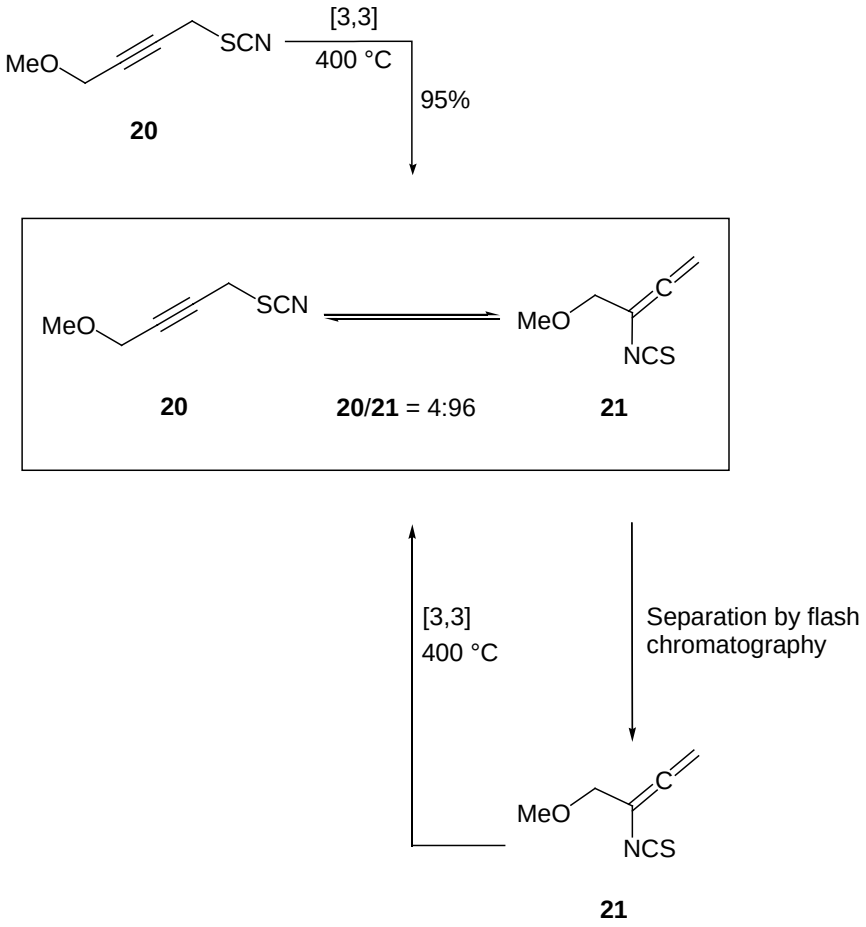
Scheme 12

Because ITC **4a** is easily accessible, it has been used as an electrophilic precursor for most of the reactions in order to investigate its reactivity with different nucleophiles and to synthesize newly substituted thiazoles. These studies will be mentioned in detail after the presentation of the FVP and/or thermolysis in solution of the other propargyl thiocyanates and enynyl ITC.

2.1.2 FVP of 1-Methoxy-4-thiocyanato-but-2-yne 20

In this study, the sigmatropic isomerization of the propargyl thiocyanate[20] **20** into allenyl ITC **21** was investigated at 400 °C and 10^{-5} Torr (Scheme 13). The equilibrium ratio between the two compounds was found to be **20/21** = 4:96, and the overall yield was 95%. Treatment of the isolated ITC **21** with gas-phase thermolysis revealed the same equilibrium

ratio between compound **21** and **20**. The obtained allene **21** was less reactive than **4a** (Scheme 13) and could be collected as a neat product. However, it cannot stay for a long time at room temperature and should be added as quickly as possible to a succeeding reaction mixture. ITC **21** is stable in solution (10%) for several weeks at –18 °C.



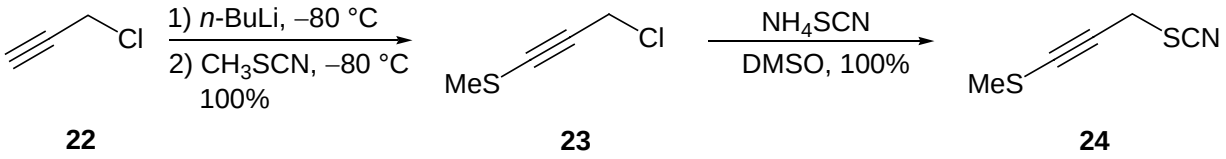
Scheme 13

2.1.3 Synthesis and FVP of 1-Methylsulfanyl-3-thiocyanato-prop-1-yne 24

2.1.3.1 Synthesis of 1-Methylsulfanyl-3-thiocyanato-prop-1-yne 24

3-Chloro-1-methylsulfanyl-prop-1-yne **23** was quantitatively prepared by deprotonation[21] of propargyl chloride **22** with *n*-butyllithium (THF/Et_2O, –80 °C) followed by electrophilic trapping with thiocyanatomethane (Scheme 14). Substitution product **24** was also prepared

quantitatively upon treatment of compound **23** with an excess of ammonium thiocyanate in DMSO for 2.5 h at room temperature.



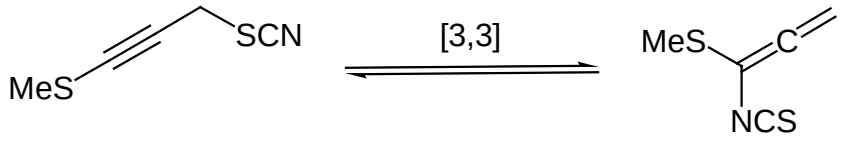
22 **23** **24**

Scheme 14

2.1.3.2 FVP of 1-Methylsulfanyl-3-thiocyanato-prop-1-yne 24

The target of this study was to investigate the effect of sulfur as a heteroatom, which is connected directly to acetylenic carbon C-1, on the [3,3] sigmatropic isomerization of propargyl thiocyanate **24** to allene **25** and on the reactivity and the stability of this allenyl ITC **25**.

In this connection, the rearrangement of compound **24** to functionalized allene **25** was studied at different temperatures (300, 350, and 400 °C) under reduced pressure (3×10^{-5} Torr) via the FVP technique (Table 2). The best ratio between **24** and **25** was found at 350 °C.



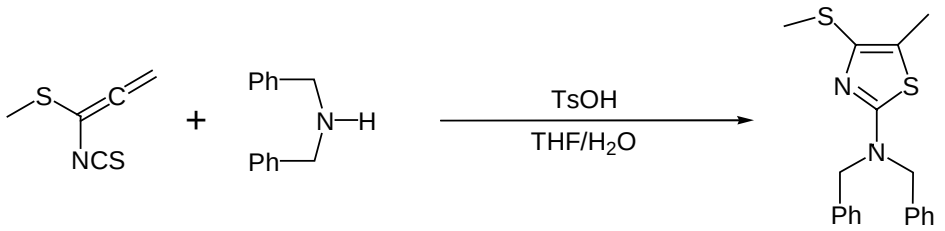
24 **25**

Table 2

Temperature (°C)	Composition of Products (%)		Yield (%)
	24	**25**	
300	73	27	95
350	18	82	93
400	31	69	30

The obtained ITC **25** was found to be highly reactive and unstable due to the electron-donating effect of the sulfur atom, which sped up the polymerization process to a few hours at room temperature in a diluted solution and to a few minutes as a neat substance. For this reason, it was impossible to measure the thermal equilibrium starting with the isolated allene **25**.

However, analytical methods (^{1}H, ^{13}C NMR, and infrared spectroscopy) confirmed the structure of allene **25**. The ^{13}C NMR spectrum of the crude reaction mixture was measured at –50 °C in $CDCl_3$, which revealed signals of the isothiocyanato group (NCS) and the central allenic carbon at 137.2 and 205.8 ppm, respectively. The characteristic absorption band of the isothiocyanato group (NCS) in the infrared spectroscopy appeared at 2038 cm^{-1}. Additionally, trapping of allene **25** with *N*,*N*-dibenzylamine **26** in the presence of toluene-4-sulfonic acid monohydrate afforded the new substituted thiazole **27** in 37% yield (Scheme 15).



25 **26** **27** (37%)

Scheme 15

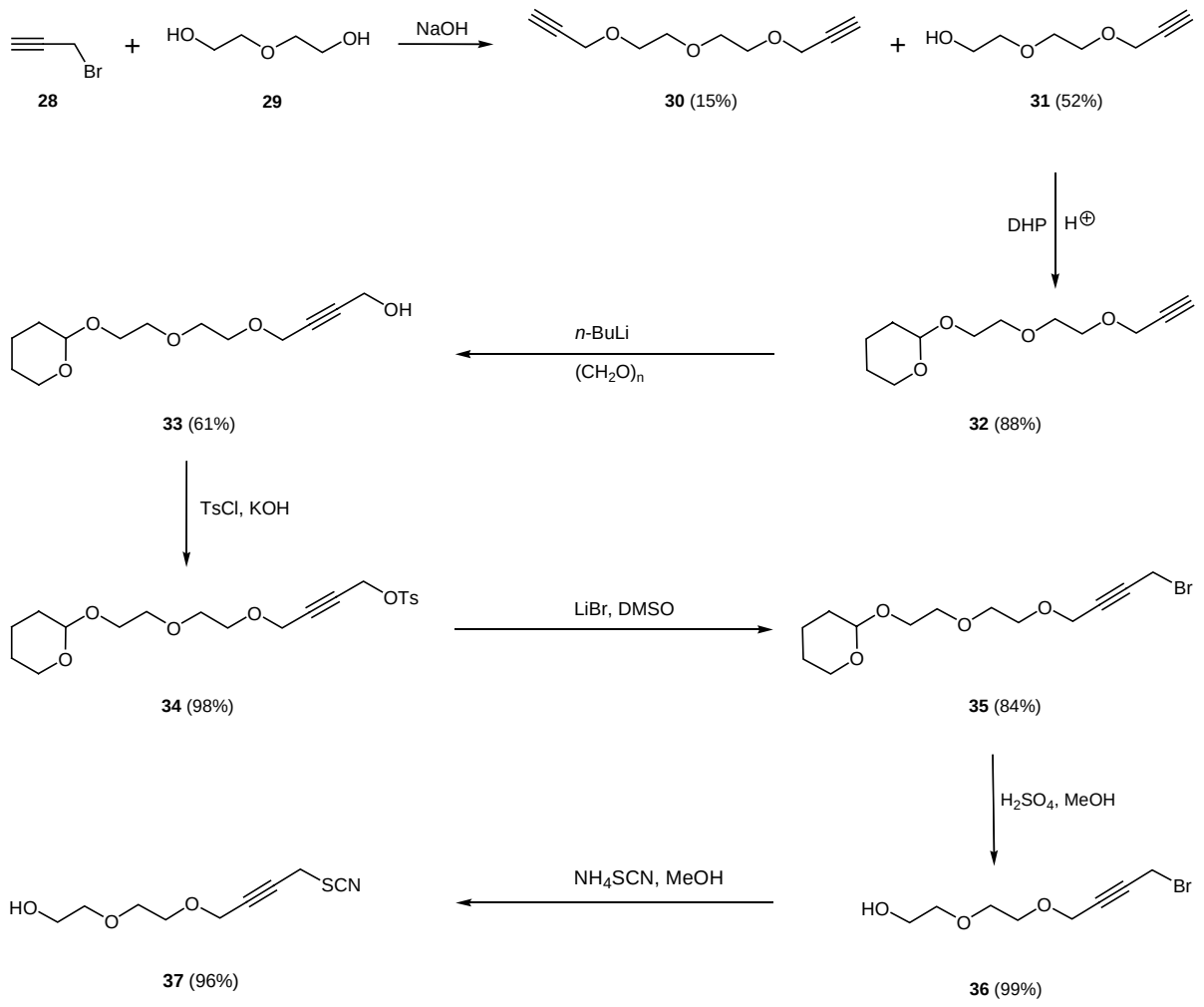
The formation of thiazole **27** was another strong evidence for the presence of the highly reactive allenyl ITC **25**.

2.1.4 Synthesis of 2-[2-(4-Thiocyanato-but-2-ynyloxy)-ethoxy]-ethanol 37 and its Thermolysis in Solution

2.1.4.1 Synthesis[22,25,26] of 2-[2-(4-Thiocyanato-but-2-ynyloxy)-ethoxy]-ethanol 37

The reaction[22] of propargyl bromide **28** with diethylene glycol **29** under controlled conditions afforded the known compounds **30**[23] and **31**[24] in 15% and 52% yields, respectively (Scheme 16). The protected alcohol **32** was synthesized[25] from hydroxy-containing compound **31** by acid catalyzedreaction with 3,4-dihydro-2*H*-pyran (DHP) in 88% yield. Propargyl alcohol **33**

was prepared[22] (61% yield) by deprotonation of alkyne **32** with *n*-BuLi (THF, –78 °C) followed by nucleophilic addition to paraformaldehyde. Treatment[26] of alcohol **33** with *p*-toluenesulfonyl chloride and KOH in diethyl ether resulted in propargyl tosylate **34** with a yield of 98%.



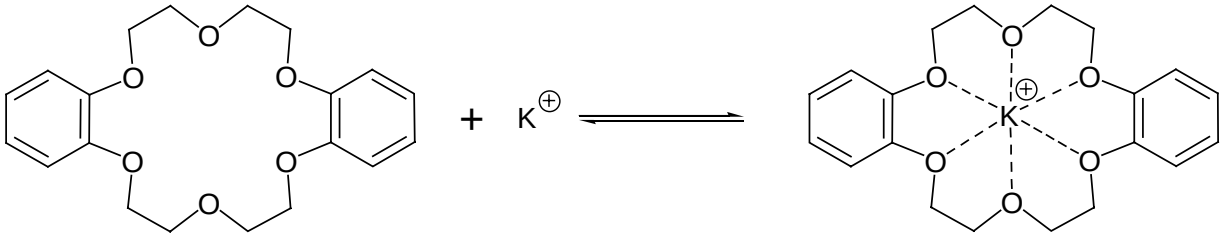
Scheme 16

Protected propargyl bromide **35** was prepared[26] in good yield (84%) upon treatment of alkyne **34** with anhydrous lithium bromide in dry DMSO for 1 h at room temperature. Deprotection[25] of compound **35** involved the use of concentrated sulfuric acid in methanol for 1 h at room temperature to reveal almost quantitatively compound **36** in 99% yield. Finally, propargyl thiocyanate **37** was also synthesized nearly quantitatively (yield 96%) after treatment of compound **36** with ammonium thiocyanate in methanol for 18 h at room temperature.

The ^{13}C NMR spectrum (in $CDCl_3$) of propargyl thiocyanate **37** revealed characteristic signals at 78.4 ppm, 83.2 ppm (both C≡C), and 110.8 ppm (SCN), while the IR spectroscopy showed two absorption bands at 3590 cm^{-1} (OH) and 2160 cm^{-1} (SCN).

2.1.4.2 Thermolysis of 2-[2-(4-Thiocyanato-but-2-ynyloxy)-ethoxy]-ethanol 37 in Solution

Crown ethers are cyclic polymers of ethylene glycol or its derivatives (Scheme 17).[27] Pedersen reported the preparation of the first crown ether, dibenzo-18-crown-6 (**DB18C6**) as well as its unique properties in 1967.[27,28]

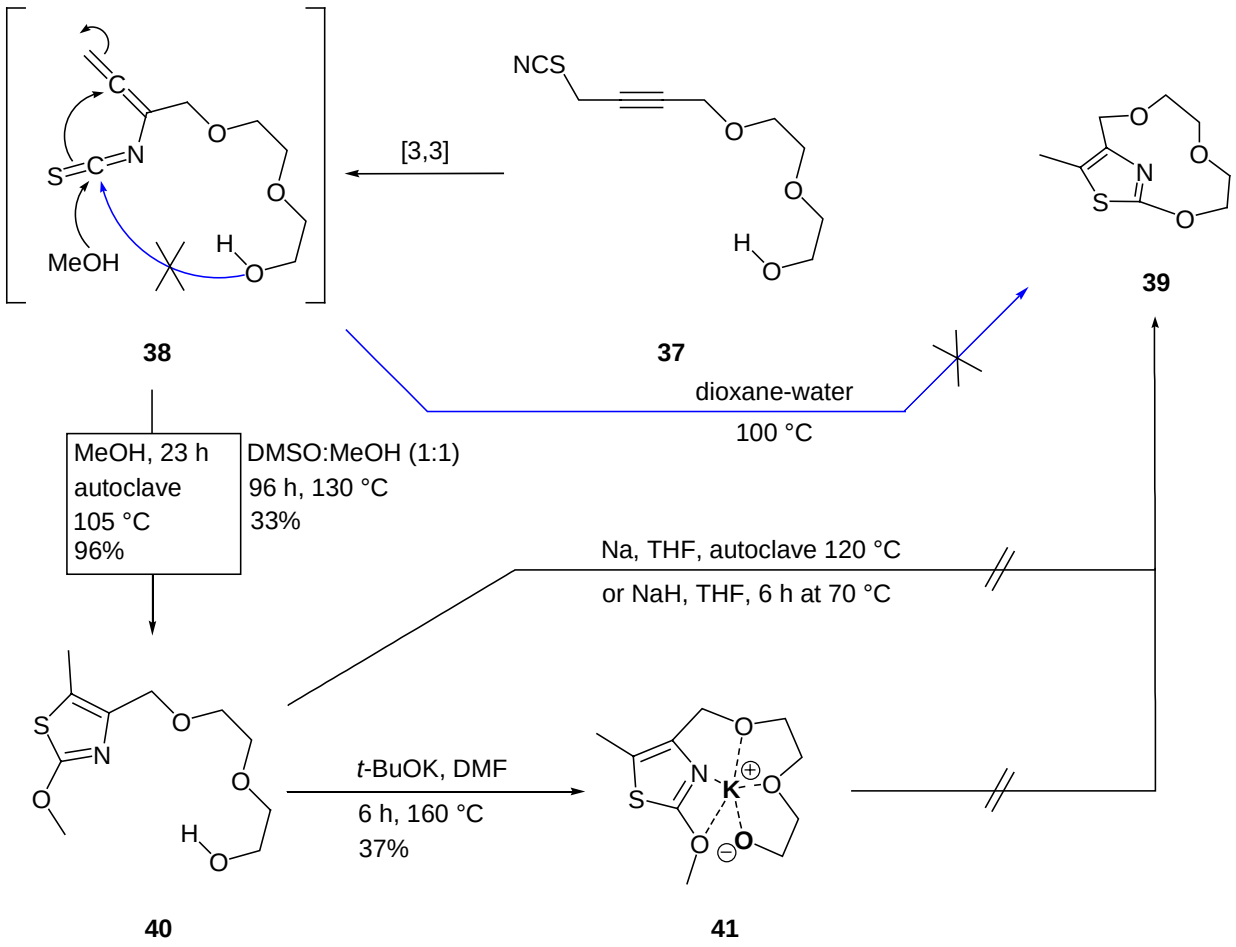


DB18C6 **DB18CH6-K⊕**

Scheme 17

This crown ether and many others have high selectivity and appreciable binding strength towards alkali and alkaline earth metal ions. For these two reasons, synthetic crown ethers mimic many properties of naturally occurring compounds. Additionally, they are important ligands not only in high-power batteries but also in isotope chemistry and radiochemistry. Moreover, they can be used in a wide range of areas such as recovery or removal of specific species, separations, ion selective electrodes, and reaction catalysts.[29]

Because of the importance and versatility of crown ethers and their derivatives, the idea was born to synthesize and investigate the [3,3] sigmatropic rearrangement of propargyl thiocyanate **37** in solution, hoping to result in intramolecular cyclization reaction via the nucleophilic attack of the terminal hydroxyl group at the intermediate allenyl ITC **38** to form the crown-ether like compound **39** (Scheme 18).



Scheme 18

Unfortunately, the thermolysis in solution of compound **37** in a dioxane-water mixture (1:1) at 100 °C did not reveal the macrocycle **39**, even in a highly diluted solution. However, we found an alternative method not only to prove the formation of intermediate **38** via [3,3] sigmatropic isomerization, but also to try preparing compound **39**. For this, substrate **37** was thermolyzed in a solution mixture of DMSO and methanol (1:1) at 130 °C for 96 h, which afforded thiazole **40** in 33% yield (Scheme 18). A convenient method of preparing compound **40** was executed by heating substrate **37** with methanol at 105 °C in an autoclave for 23 h. In this way, we confined the reaction of allene **38** with methanol only, rather than polymerization, to give thiazole **40** in a very good yield (96%). These results were consistent with the formation of the allene **38**, which reacted with the methanol under specific conditions to give compound **40** (see the experimental section).

Many cyclization methods are based on the use of a temporary or permanent template and on specific ring closure reactions, which depend on the nature of the reacting groups.[30] Thus, numerous attempts were carried out to prepare crown ether **39** by reacting methoxy thiazole **40** with Na in THF under high temperature and pressure. Even with NaH in THF at 70 °C, attempts ended with the formation of unknown products only. Additionally, heating of thiazole **40** with *t*-BuOK in dry DMF at 160 °C for 72 h gave a mixture of unknown products.

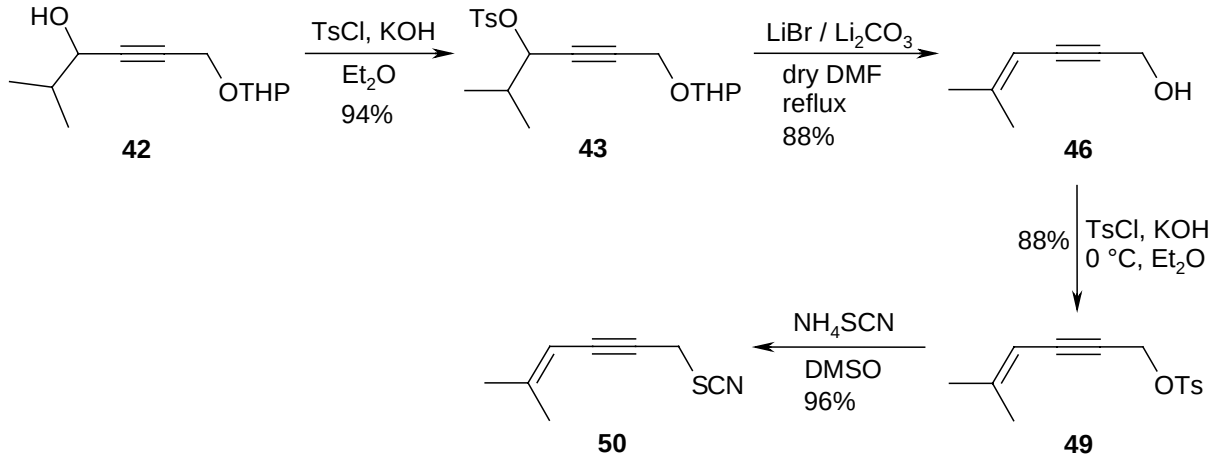
Surprisingly, in treating the methoxy thiazole **40** with *t*-BuOK in dry DMF at 160 °C for 6 h revealed the macrocyclic complex **41** in a 37% yield. Presumably, the formation of sterically favored complex **41**, rather than compound **39**, may be explained by the low nucleophilicity of the terminal ethoxide anion, which was reduced by interaction with the K^+ cation, in addition to the presence of the methoxy group, which is not a reactive leaving group. Physical methods (^1H and ^{13}C NMR in $CDCl_3$) showed a highfield chemical shift of the methoxy group by 0.7 ppm and 28 ppm in the ^1H and ^{13}C NMR spectra, respectively, in comparison with the starting material **40**. This may be attributed to the affect of the electron density of the ethanolate substructure, which is very close to the methoxy group. Further, the MS spectrum showed an increase in the molecular weight of compound **41** by 39 units.
These concurrent changes in the ^1H NMR, ^{13}C NMR, and MS spectra led us to conclude that the K^+ cation made coordination bonds with the five heteroatoms to form the crown-ether like compound **41**.

2.1.5 Synthesis and Reactions of 2-Methyl-6-thiocyanato-hex-2-en-4-yne 50

2.1.5.1 Synthesis[31–38] of 2-Methyl-6-thiocyanato-hex-2-en-4-yne 50

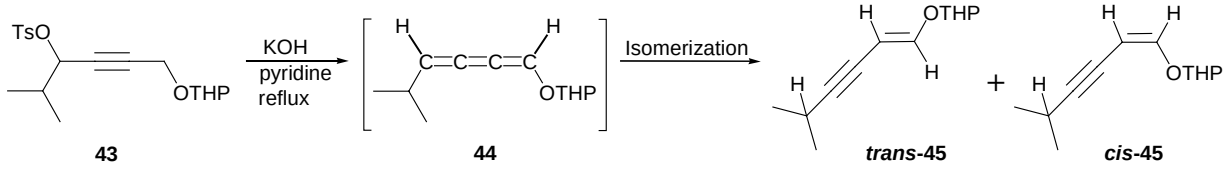
Many unsuccessful attempts were carried out to prepare toluene-4-sulfonic acid 1-isopropyl-4-(tetrahydro-pyran-2-yloxy)-but-2-ynyl ester **43** by using a modified known procedure (pyridine with tosyl chloride and ethyl acetate,[31] Scheme 19). On the other hand, in treating[32] the 2-methyl-6-(tetrahydro-pyran-2-yloxy)-hex-4-yn-3-ol **42**[33] with *p*-toluenesulfonyl chloride in diethyl ether using a strong base (KOH) afforded **43** in very good yield (94%). Numerous unsuccessful trials were executed to prepare 5-methyl-hex-4-en-2-yn-1-ol **46**[34]

either by refluxing **43** with KOH in diethyl ether[32] or with KOH and pyridine. Mild conditions, stirring of **43** with KOH and pyridine overnight, followed by heating for 5 h at 40°C and then heating for 2 h at 70 °C were unsuccessful.



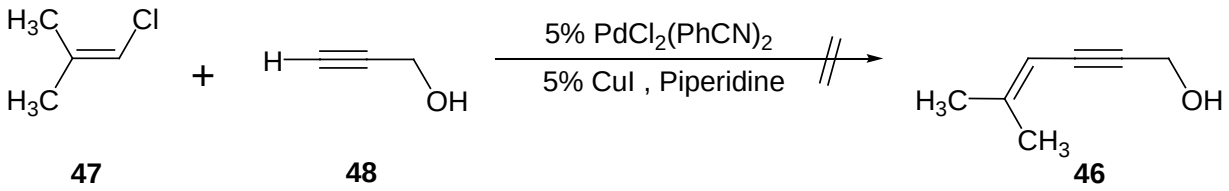
Scheme 19

Indeed, refluxing **43** with KOH and pyridine afforded two unexpected isomers 2-(5-methyl-hex-1-en-3-ynyloxy)-tetrahydro-pyran *trans*-**45** and *cis*-**45**, respectively, which resulted most propably from the rearrangement of triene intermediate **44**[35,36] (Scheme 20). The intermediate **44** came out through the 1,4-elimination of TsO–H of compound **43** under the above-mentioned conditions. The structure of the two isomers was proved by the physical analyses.



Scheme 20

Actually, 5-methyl-hex-4-en-2-yn-1-ol **46**[34] could not be prepared by Pd^{+2} catalyzed coupling of 1-chloro-2-methyl-1-propene **47** and propargyl alcohol **48** following the procedure reported by Alami et al.[37] (Scheme 21).



Scheme 21

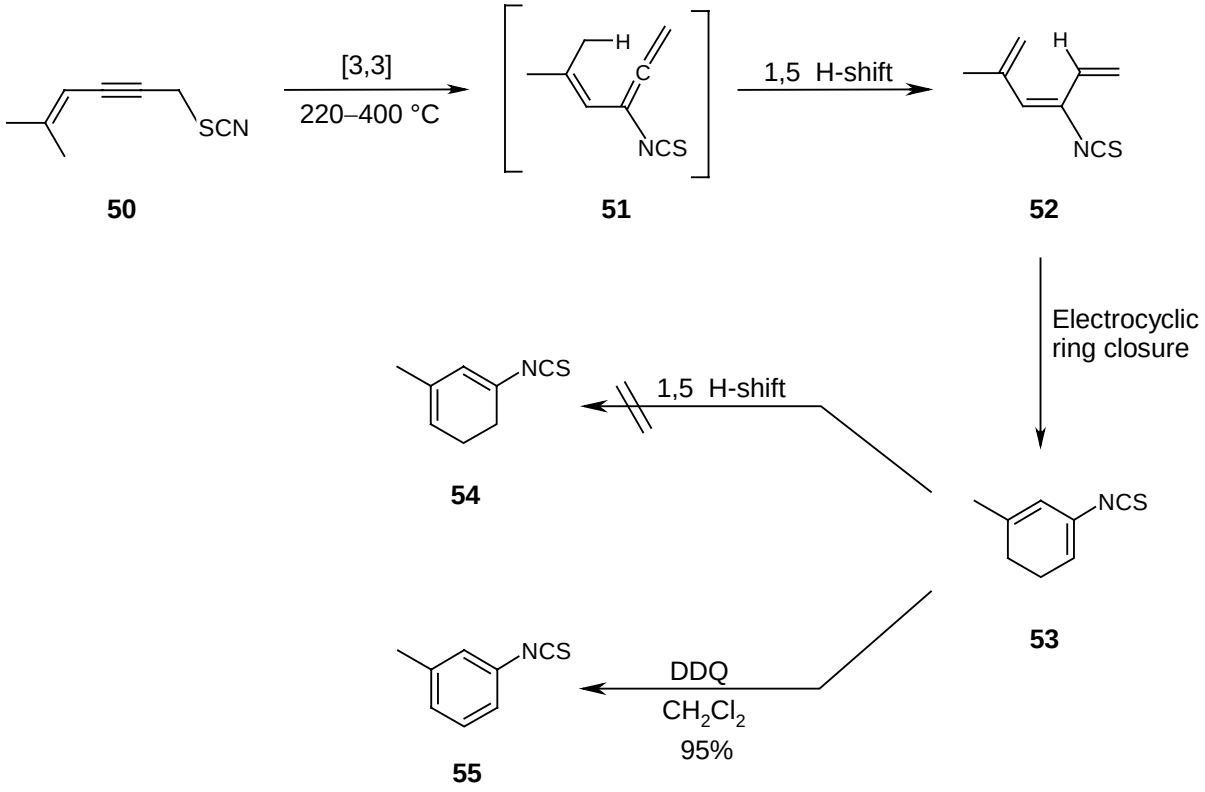
It was found that the simultaneous 1,2-elimination of the TsO–H group and the deprotection of the desired compound **43** could be done best by using anhydrous lithium bromide and lithium carbonate in dry DMF,[38] which gave **46**[34] in very good yield (88%), see Scheme 19.

Treatment[32] of **46**[34] with *p*-toluenesulfonyl chloride and KOH at low temperature gave toluene-4-sulfonic acid 5-methyl-hex-4-en-2-ynyl ester **49** in 88% yield, which reacted with ammonium thiocyanate in DMSO to afford 2-methyl-6-thiocyanato-hex-2-en-4-yne **50** with 96% yield. The ^{13}C NMR of **50** (in $CDCl_3$) revealed two characteristic signals of the methylene group (-CH_2-SCN) and thiocyanate group (SCN) at 24.8 and 111.2 ppm, respectively, while the methylene group (-CH_2-OTs) of **49** appeared at 59.0 ppm. The infrared absorption spectrum of **50** showed a characteristic absorption band of SCN at 2159 cm^{-1}.

2.1.5.2 FVP of 2-Methyl-6-thiocyanato-hex-2-en-4-yne 50

The goal of this system was to study the mechanistic process of [3,3] sigmatropic rearrangement of the conjugated thiocyanate **50** and its succeeding reactions using the FVP technique and thermolysis in solution.

Flash vacuum pyrolysis of **50** at 400 °C and 10^{-5} Torr gave 3-isothiocyanato-1-methyl-cyclohexa-1,3-diene **53** as a colorless liquid in 91% yield (Scheme 22). Compound **53** readily changes to a green-yellow color upon contact to air.



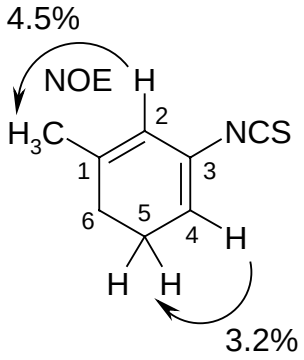
Scheme 22

Similar FVPs of **50** were also carried out at lower temperatures and resulted in unchanged 2-methyl-6-thiocyanato-hex-2-en-4-yne **50**, *E*-4-isothiocyanato-2-methyl-hexa-1,3,5-triene **52**, and additionally 3-isothiocyanato-1-methyl-cyclohexa-1,3-diene **53** as mixtures (Table 3).

Table 3

Temperature / °C	Composition of products (%)				Yield (%)
	50	**51**	**52**	**53**	
400	0	0	0	100	**91**
350	1	0	0	99	**91**
300	68	0	20	12	**88**
270	69	0	15	16	**85**
220	95	0	4	1	**91**

Many attempts to trap 3-isothiocyanato-5-methyl-hexa-1,2,4-triene **51** with help of nucleophile (MeOH) were unsuccessful due to its high reactivity. It was even impossible to detect the intermediate **51**, which was formed via [3,3] sigmatropic rearrangement and underwent 1,5 hydrogen shift to reveal the conjugated triene **52**, in the NMR experiments (compare Scheme 22). The electrocyclic ring closure of triene **52** afforded diene **53**. The structure of isothiocyanate **53** was also assigned by homonuclear NOE difference spectra (Scheme 23) in order to exclude 1-isothiocyanato-3-methylcyclohexa-1,3-diene **54**, which may have resulted from a further 1,5 hydrogen shift of **53** (see Scheme 22).



53

Scheme 23

The only possible stereochemistry of the conjugated triene **52** was the *E*-configuration; otherwise it would be difficult to undergo the electrocyclic ring closure. The intramolecular 1,5 hydrogen shift of **51** could only result in *E*-configuration of **52**. Additionally, only one isomer of triene **52** was detected by the NMR spectroscopy.

2.1.5.3 Thermolysis of 2-Methyl-6-thiocyanato-hex-2-en-4-yne 50 in Solution

Three isomers **50**, **52**, and **53** were also detected, in comparison with FVP, by thermolysis of a solution of propargyl thiocyanate **50** in toluene-d_8 at 115 °C, while it was impossible to detect the highly reactive intermediate allene **51** (Table 4 and Scheme 22). Surprisingly, after 20 h at 115 °C, only compound **53** could be detected by NMR (62% yield, grease was used as a standard).

Table 4

Time (min)	Composition of products (%)[a]		
	50	**52**	**53**
0	100	0	0
10	100	0	0
30	97	3	0
60	94	5	1
100	87	9	4
140	80	13	7
190	76	15	9
240	67	19	14
276	57	21	22
345	45	25	30
365	39	23	38
480	32	20	48
600	26	17	57

[a]Between the times 0–600 min, the presented percentages reflect the product composition up to the standard compound (grease).

The relationship between composition of products (%) and the time (min) after 600 min is shown in Figure 2.

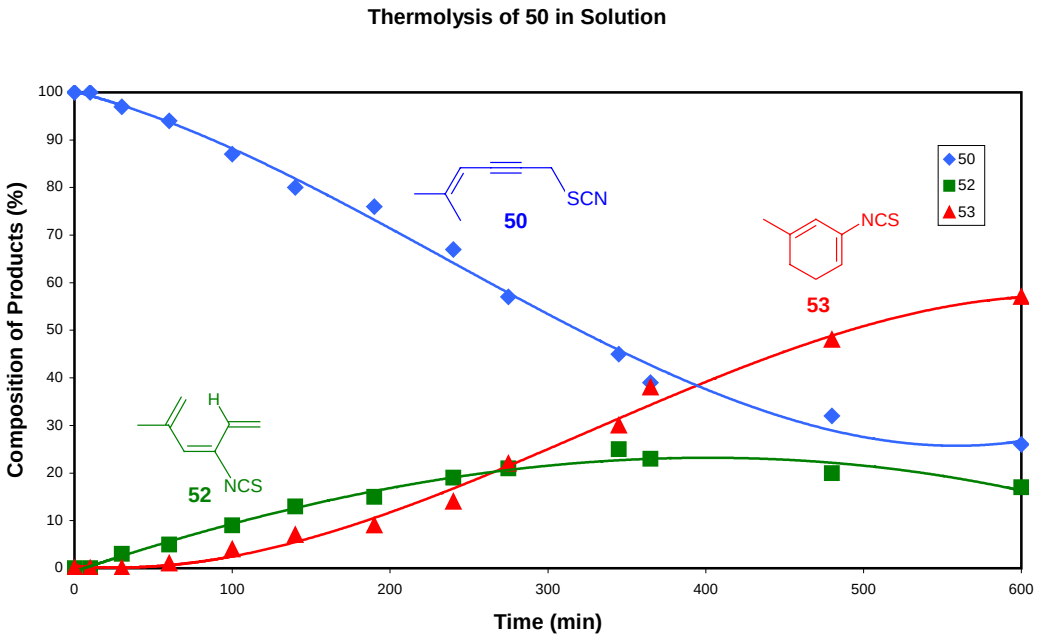


Figure 2

2.1.5.4 Oxidation of 3-Isothiocyanato-1-methyl-cyclohexa-1,3-diene 53

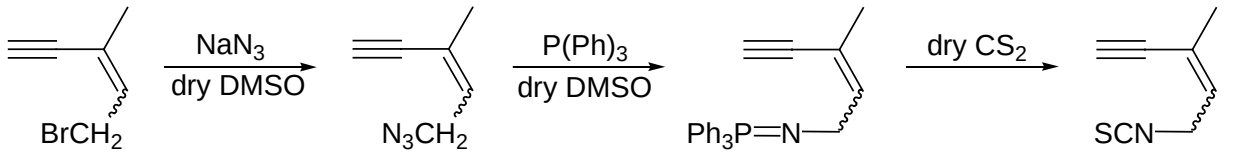
To confirm the structure and to prepare a stable derivative of ITC **53**, it was oxidized in the presence of 4,5-dichloro-3,6-dioxo-cyclohexa-1,4-diene-1,2-dicarbonitrile (DDQ) within three hours at 50 °C in dry dichloromethane to furnish nearly quantitatively (95%) the commercially available 1-isothiocyanato-3-methyl-benzene **55** (Scheme 22).

2.1.6 Synthesis and FVP of *Z/E*-1-Isothiocyanato-3-methyl-pent-2-en-4-yne 59

2.1.6.1 Synthesis[39–41] of Z/E-1-Isothiocyanato-3-methyl-pent-2-en-4-yne 59

Z/E-Isothiocyanates **59** were prepared in a one-pot reaction with a very good yield (Scheme 24). Treating *Z/E*-1-bromo-3-methyl-pent-2-en-4-yne **56**[39] with sodium azide in dry DMSO gave *Z/E*-1-azido-3-methyl-pent-2-en-4-yne **57**,[40] which were transferred into *Z/E*-3-methyl-1-(triphenylphosphora-nylideneamino)-pent-2-en-4-yne **58** immediately by Staudinger's method[41] (the reaction of triphenyl phosphine with the corresponding azides **57**). Finally, addition of an excess amount of dry carbon disulfide to *Z/E*-iminophosphoranes **58** produced

the target molecules ITCs **59** as geometrical isomers ***Z*-59** and ***E*-59** in ca. 13:1 ratio and 84% overall yield.



***Z,E*-56** ***Z,E*-57** ***Z,E*-58** ***Z,E*-59** 84% based on ***Z,E*-56**

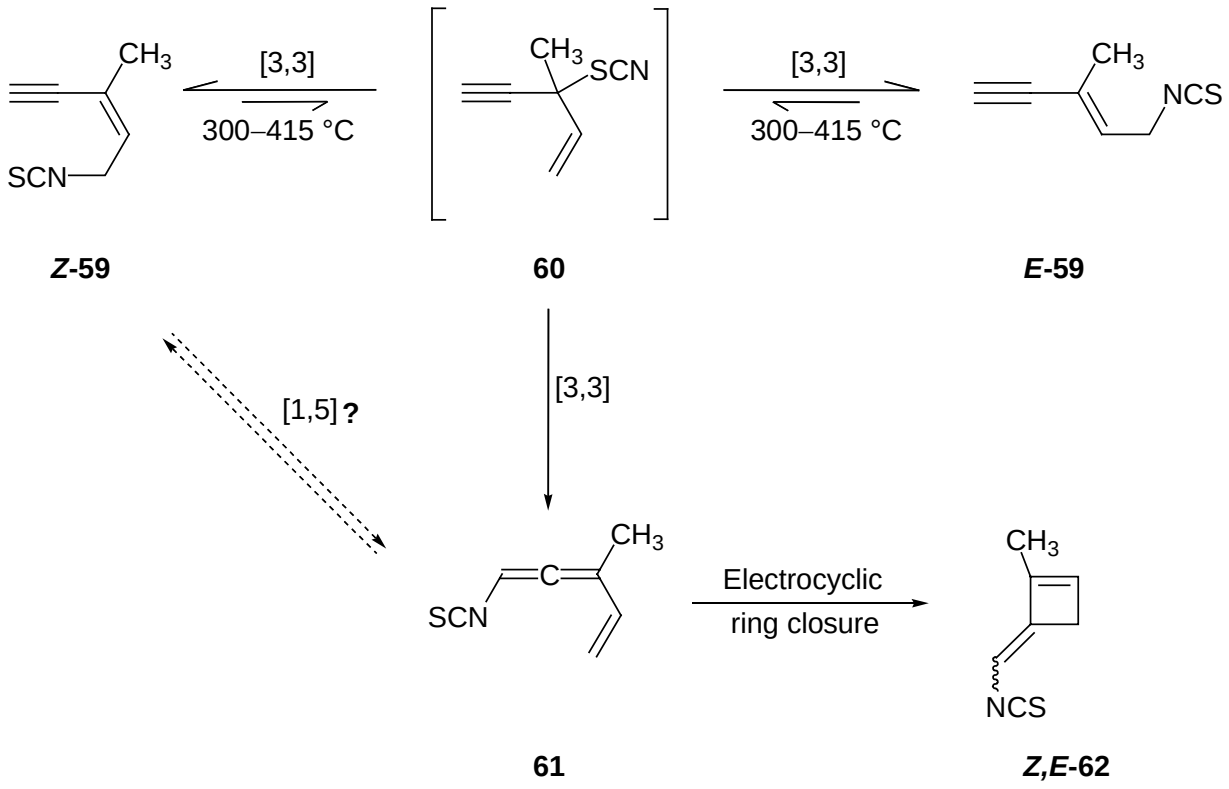
Scheme 24

Compounds **57** and **58** were detected by executing the experiment in a NMR tube using dry d_6-DMSO as solvent.

2.1.6.2 FVP of Z/E-1-Isothiocyanato-3-methyl-pent-2-en-4-yne 59

The aim of this part of the present research was to investigate the double [3,3] sigmatropic rearrangement and reaction mechanism of the conjugated enynyl ITCs **59**, which revealed new ITCs derivatives.

Flash vacuum thermolysis of a mixture of geometrical isomers ***Z/E*-59** was performed at 300, 350, 400 and 415 °C and 10^{-2} Torr to yield mixtures of unchanged ***Z/E*-59**, **61**, and ***Z/E*-62** with different ratios (Table 5 and Scheme 25). The intermediate 3-methyl-3-thiocyanto-pent-1-en-4-yne **60**, which was furnished as a result of [3,3] sigmatropic rearrangement of isomers ***Z/E*-58**, was not detected due to its high reactivity. Nevertheless, the [3,3] sigmatropic rearrangement reaction of thiocyanate **60** afforded the allenyl ITC **61**, which underwent electrocyclic ring closure to give geometrical isomers ***Z/E*-62** with ca. 1:1 ratio. Despite this, many unsuccessful trials were made to trap compound **61** with the help of nucleophile (MeOH). On the other hand, the [1,5] sigmatropic migration of the ITC group of ***Z*-59** to the allenyl ITC **61** may have been a competing reaction.



Scheme 25

The ratio between geometrical isomers ***Z/E*-62** was ca. 1:1 at 300 °C and 415 °C (Table 5). However, the yield of the resulting mixtures (***Z/E*-59**, **61**, and ***Z/E*-62**) decreased as the temperature increased. This may be ascribed to the decomposition of the corresponding ITCs ***Z/E*-62**. It was found that the suitable temperature for generating ***Z/E*-62** with best yield was 400 °C (Table 5). On reacting isomers ***Z/E*-62** with different type of nucleophiles to prepare derivatives, a mixture of unknown products were produced.

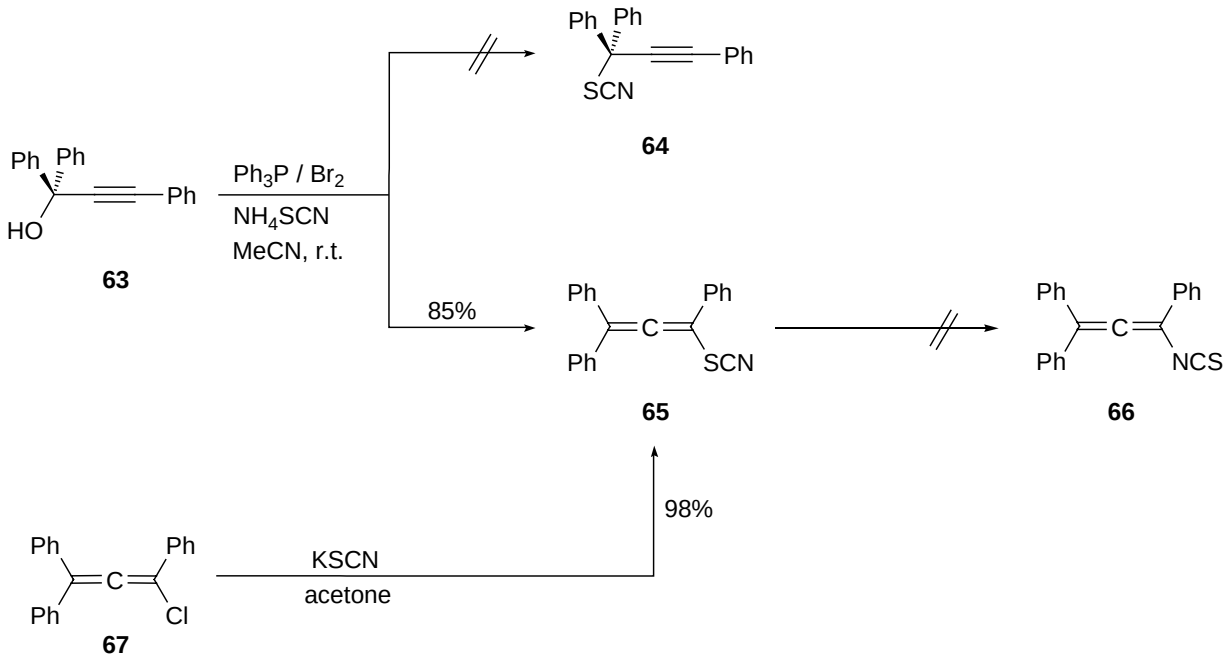
Table 5

Temperature / °C	Composition of products (%)					Yield (%)
	***Z*-59**	***E*-59**	**61**	***Z*- *or E*-62**	***Z*- *or E*-62**	
300	73	19	4	2	2	**83**
350	24	6	12	32	26	**80**
400	10	3	8	42	37	**75**
415	3	0	0	50	47	**50**

2.1.7 Preparation of 1,3,3-Triphenylallenyl Thiocyanate 65[43]

N. Iranpoor et al.[42] reported an efficient one-pot thiocyanation of tertiary alcohols by *in situ* generation of $Ph_3P(SCN)_2$. The reaction of 1,1,3-triphenyl-prop-2-yn-1-ol **63** with the previously mentioned $Ph_3P(SCN)_2$ furnished the allenyl thiocyanate **65**[43] with 85% yield without any detection of the propargyl thiocyanate **64** (Scheme 26). This can be attributed to the highly conjugated stable product **65** in comparison with compound **64**. However, we were unsuccessful in synthesizing the ITC **66** by making thermolysis[44] in solution (for substrate **65**) in the presence of a polar solvent (DMSO, DMF) and the catalytic effect of electrophilic agent ($ZnCl_2$).

Previously, S. Miyake and H. Taniguchi et al.[43] prepared compound **65** by solvolytic reaction of chloroallene **67** in the presence of potassium thiocyanate with 98% yield.



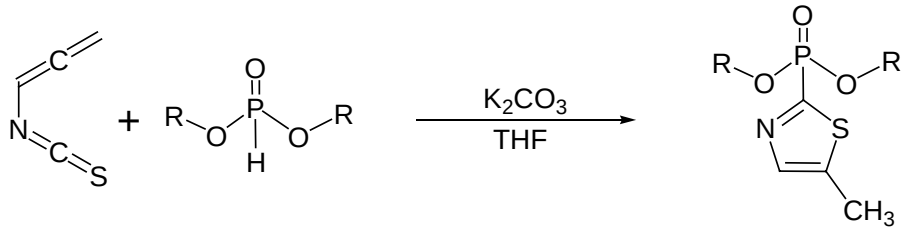
Scheme 26

2.2 Succeeding Reactions of Allenyl ITCs 4a and 21 with Different Nucleophiles: Synthesis of Substituted Thiazoles

2.2.1 Reaction of Allenyl ITC 4a with Dialkyl or Diphenyl Phosphites

Organophosphonate derivatives hold great medical and industrial importance. Medically, they have widespread application for the treatment of bone diseases and as ligands for ^{99m}Tc-based bone imaging agents.[45] Moreover, they are not only important intermediates for the synthesis of many biologically active compounds[46] but also have antiviral,[47–49] antitumoral,[49] and herbicidal activities.[50] In the industrial field, they can be used as plasticizers for polyvinyl chloride.[51]

These observations, together with a longstanding interest in a new method for P–C bond formation, led us to attempt a synthesis of new-substituted thiazoles containing phosphonate groups at C-2 position. However, treating the appropriate phosphites **68a–c** with ITC **4a** did not lead to heterocyclic products. In repeating the same reaction in the presence of potassium carbonate, which might serve as a heterogeneous catalyst, newly substituted thiazoles **69a–c** were formed with very good yields (Scheme 27).



4a **68a–c**

69a, R = CH_3 **(83%)**

69b, R = Ph **(90%)**

69c, R = CH_2Ph **(88%)**

Scheme 27

Fortunately, these are the first examples of aromatic thiazoles bearing a phosphorus atom of a phosphonate group at C-2 position of the thiazole ring. ^{1}H NMR, ^{13}C NMR, and IR

spectroscopy, in addition to the elemental analysis, were used to confirm the structures of these novel compounds.

However, the ^{1}H NMR spectrum of phosphonate **69a** showed the methoxy group as doublet with coupling constant $^{3}J_{PH}$ = 11.4 Hz, while the ^{1}H NMR spectrum of phosphonic ester **69c** showed two different types of diastereotopic hydrogens (Ha and Hb) with coupling constants $^{3}J_{PH}$ = 12 Hz, $^{3}J_{PH}$ = 11.7 Hz and $^{2}J_{Ha, Hb}$ = 8.1 Hz (Figure 3).

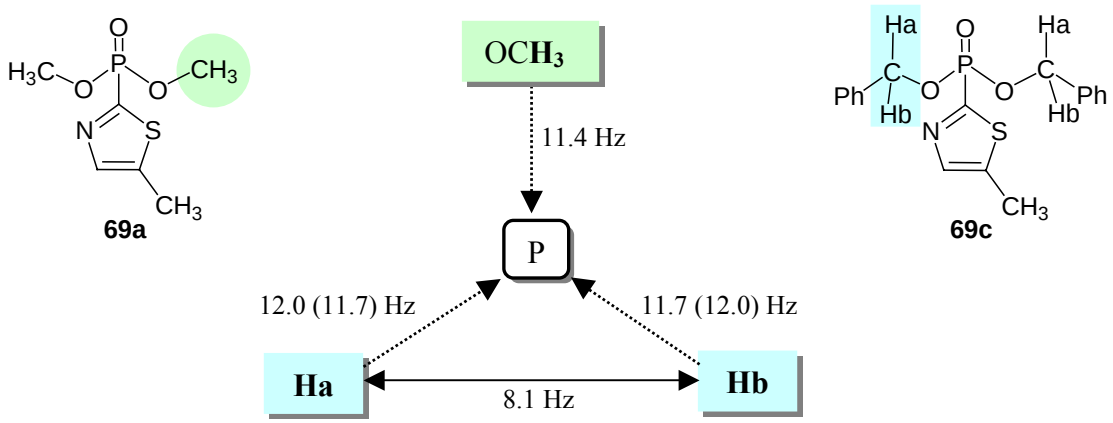


Figure 3

On the other hand, ^{13}C NMR spectra of heterocycles **69a–c** revealed the significant P–C(2) and P–C(4) couplings summarized in Table 6.

Table 6

^{13}C NMR		Compound No.		
		69a	**69b**	**69c**
C-2	$^{1}J_{PC}$ (Hz)	245.8	256.6	247.6
C-4	$^{3}J_{PC}$ (Hz)	26.2	28.4	26.8
–OCH_3	$^{2}J_{PC}$ (Hz)	6.2	----	----
–OCH_2Ph	$^{2}J_{PC}$ (Hz)	----	----	5.6
Ph_i	$^{2}J_{PC}$ (Hz)	----	7.4	----
Ph_i	$^{3}J_{PC}$ (Hz)	----	----	6.8
Ph_o	$^{3}J_{PC}$ (Hz)	----	4.6	----
Ph_m	$^{4}J_{PC}$ (Hz)	----	1.1	----

The P–C(1) coupling constants ($^1J_{PC}$) of the three phosphonates **69a–c** were consistent with the published[52] results of similar compounds. However, no coupling was detected between the P–C(5) of the thiazole moieties **69a–c**. The ^{13}C NMR spectrum of compound **69c** is shown in Figure 4.

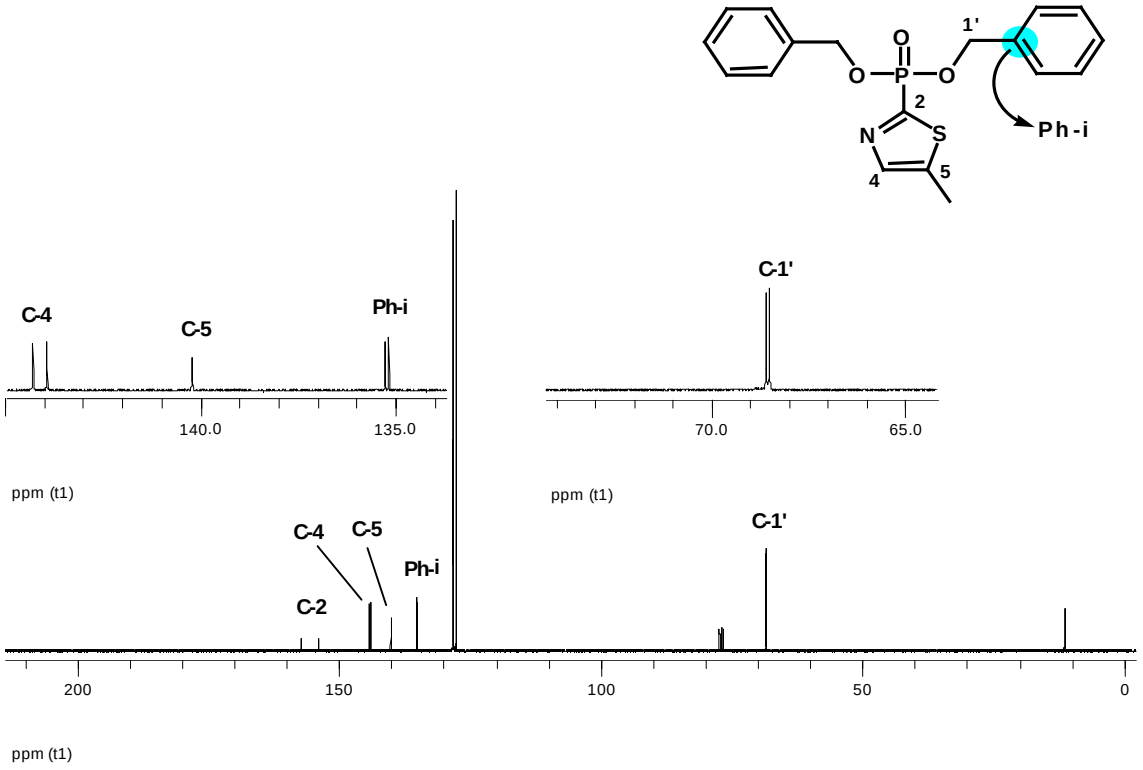
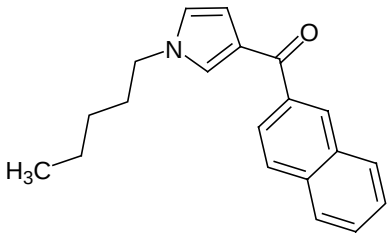


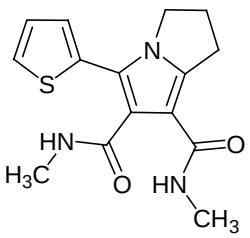
Figure 4. ^{13}C NMR spectrum of thiazole **69c**

2.2.2 Reaction of Allenyl ITC 4a with Five-Membered Ring Heteroaromatic Compounds Containing One Heteroatom

Pyrrole and thiophene derivatives are naturally occurring compounds with significant biological activities[53,54] such as pyrrole **70** and antileukemic agent **71** (Scheme 28).[55]



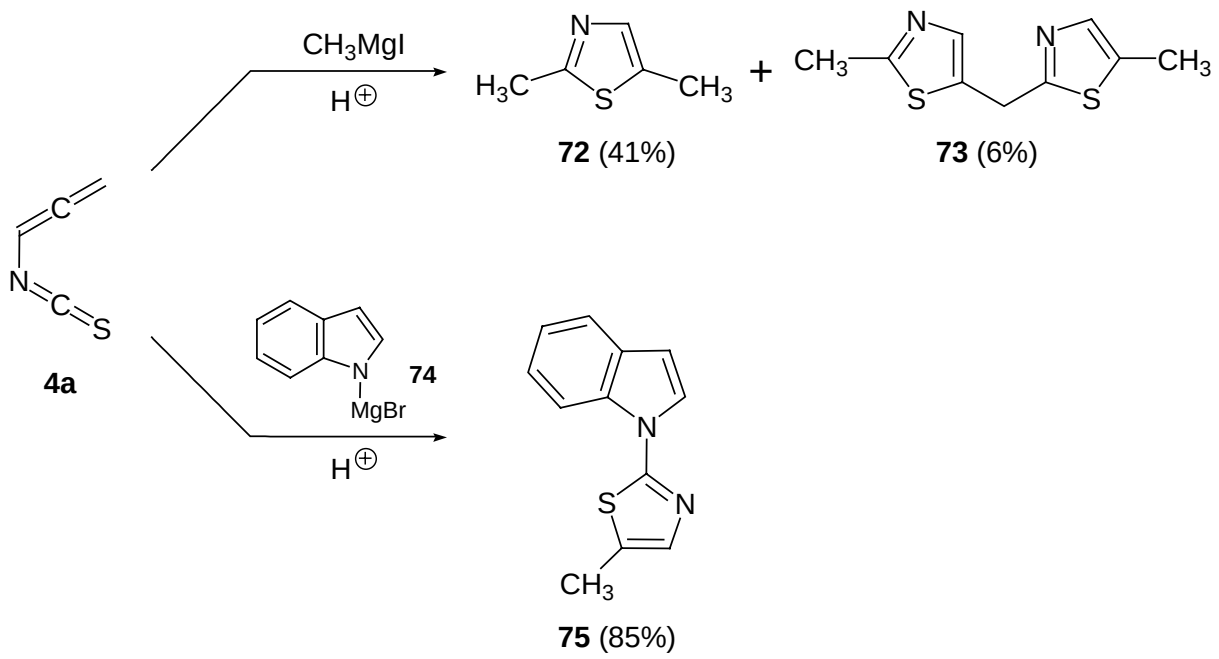
70



71

Scheme 28

It was reported that the reaction of Grignard reagents such as methylmagnesium iodide and indolylmagnesium bromide **74** with allenyl ITC **4a** gave the opportunity to synthesize thiazoles derivatives by forming one or two new C–C bonds at the same time or a new N–C bond in the cases of **72**, **73** or **75**, respectively (Scheme 29).[8a,56]



Scheme 29

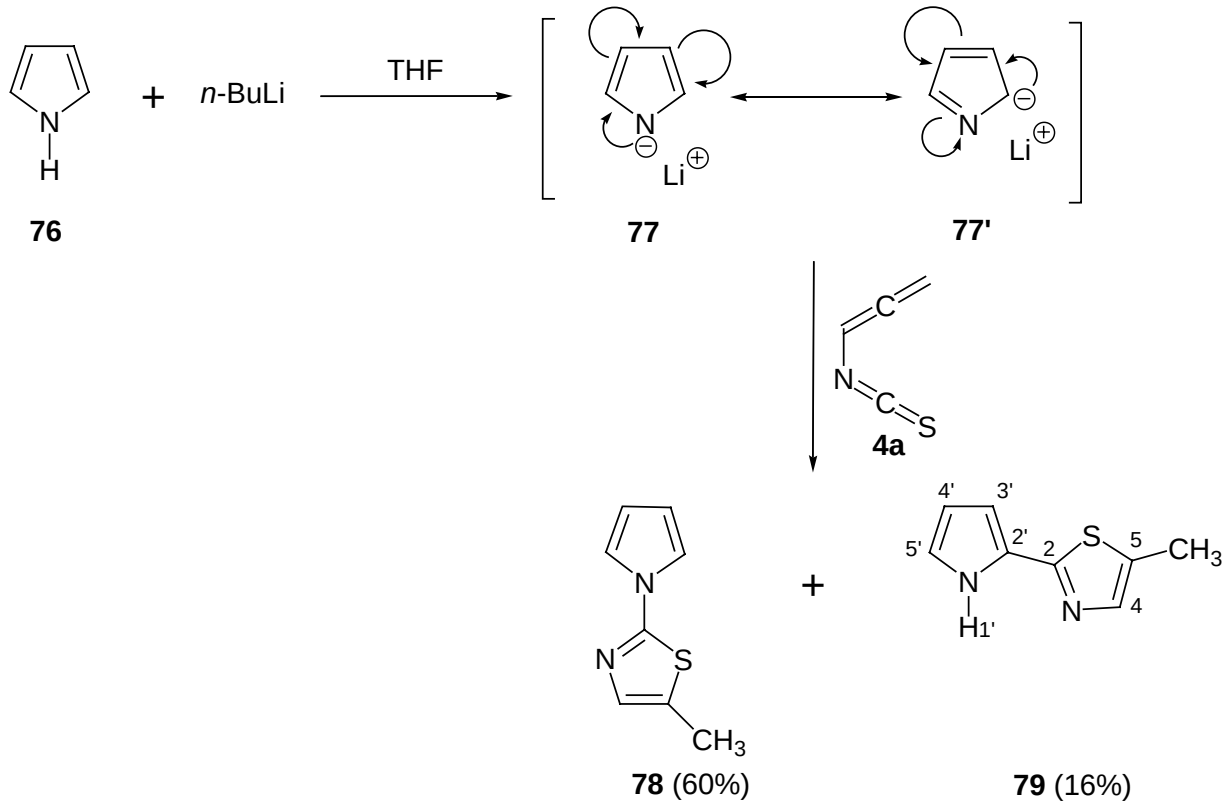
In this system, the chemistry of pyrrole and thiophene anions was studied in the presence of the highly reactive ITC **4a** in order to investigate the reaction pathway of N–C and C–C bond formation.

Because pyrrole and thiophene were unable to react directly with allenyl ITC **4a**, we prepared the organolithium salts **77** and **86**, in addition to the organomagnesium salt **80**, to be used as nucleophiles for our reactions.

2.2.2.1 Reaction of Allenyl ITC 4a with Pyrrole using Alkyllithium

Pyrrole **76** has a weakly acidic hydrogen atom attached to the nitrogen and can be deprotonated by using a strong base, like *n*-butyllithium.[57] The reaction of pyrrole **76** with

n-butyllithium gave pyrrole salt **77**, also describable in the mesomeric form **77'**, which attacks the allene **4a** to afford 5-methyl-2-pyrrol-1-yl-thiazole **78** as a result of nitrogen–carbon bond formation with 60% yield and 5-methyl-2-(1*H*-pyrrol-2-yl)-thiazole **79** due to the carbon–carbon bond formation with 16% yield (Scheme 30).



Scheme 30

The structure of substituted pyrroles **78** and **79** was proved by ^{1}H NMR, ^{13}C NMR, IR spectroscopy, and elemental analysis. The structure of compound **79** was also assigned by an archetypal method via comparing its ^{1}H NMR chemical shifts and coupling constants with the standard unsubstituted molecule of pyrrole **76**.[58] This comparison was useful not only for excluding the possibility of formation of a product bearing the thiazole ring at C-3' position, but also to have the correct assignment for the hydrogen atoms. The values of chemical shifts and coupling constants are described in Figure 5.

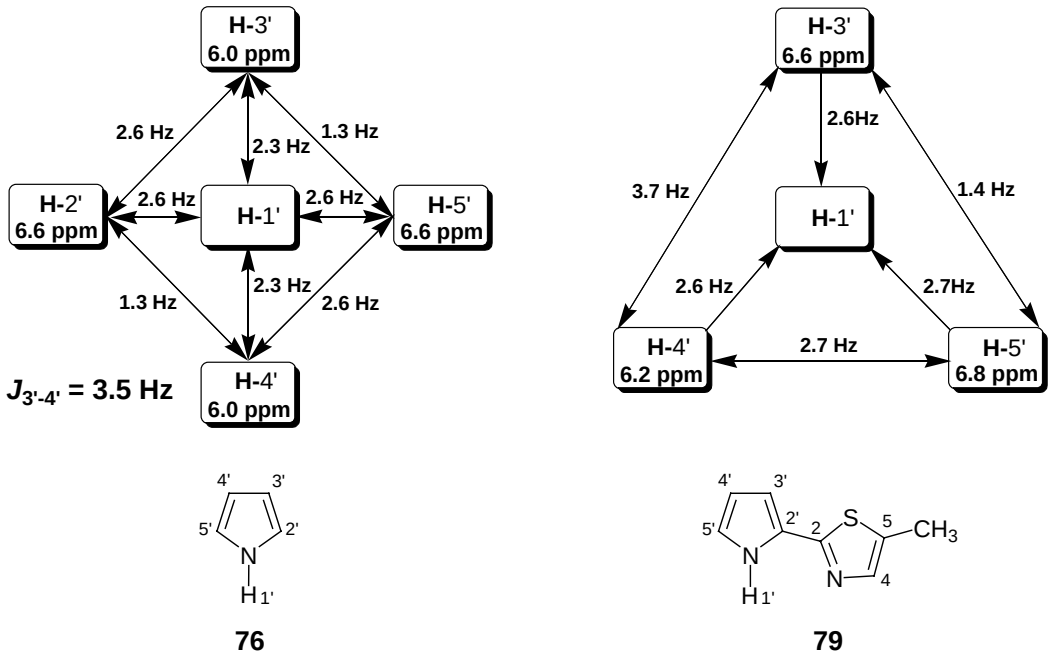


Figure 5

Obviously, the ^{1}H NMR chemical shift of H-3' of pyrrole **79** was noticeably downfield shifted due to the aromaticity of the thiazole moiety, while the coupling constant values of the whole hydrogen atoms had values analogous to parent compound **76**.

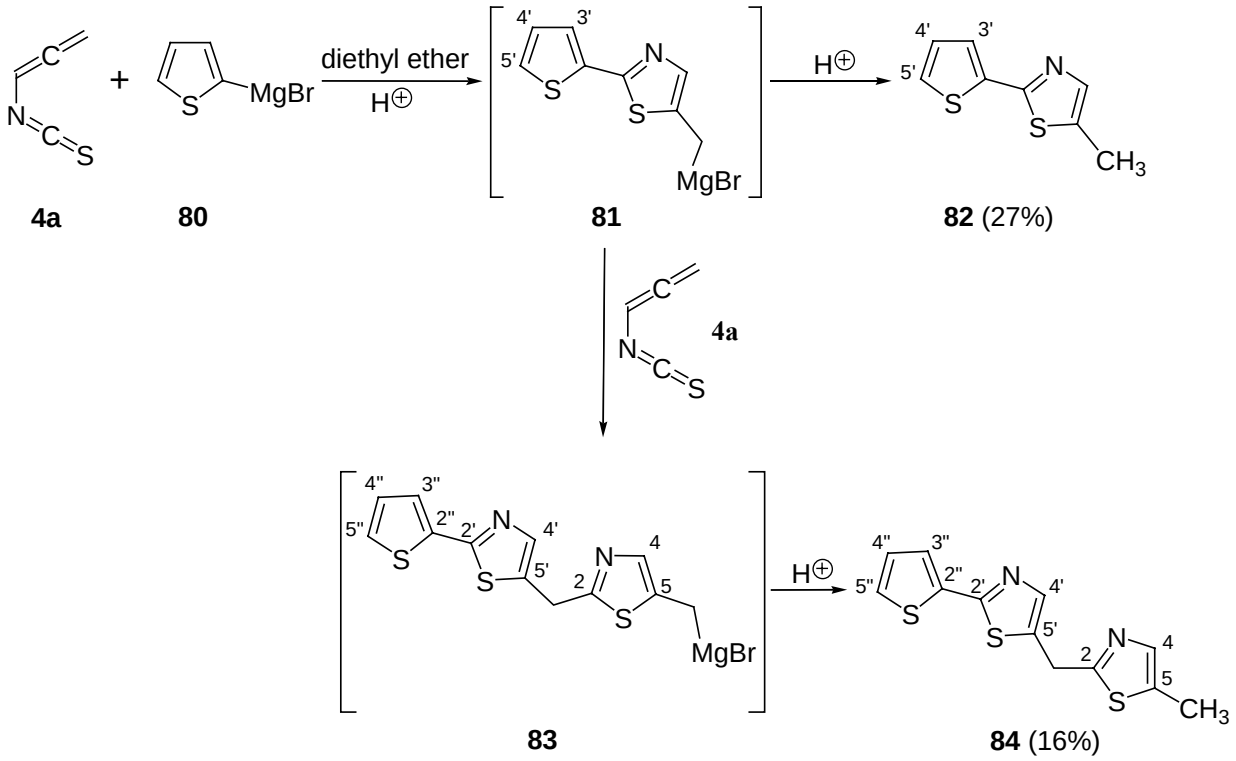
The IR spectrum of compound **79** showed a characteristic absorption band of NH at 3466 cm^{-1}. On the other hand, no absorption band could be detected in this region for the product **78** due to substituent with of thiazole moiety at N-position.

2.2.2.2 Reaction of Allenyl ITC 4a with Thienylmagnesium Bromide 80 and Thienyllithium 86

2.2.2.2.1 Reaction of Allenyl ITC 4a with Thienylmagnesium Bromide 80

Thienylmagnesium bromide **80**[59] was treated with allene **4a** at 0 ºC for 20 min in dry diethyl ether to give two different substituted thiazoles, the known thiazole **82**[60] and bis-thiazole **85** with yields of 27 and 16%, respectively (Scheme 31). Heterocycle **84** was obtained due to the nucleophilic addition of intermediate **81** to a second molecule of allene **4a** followed by protonation of magnesium bromide salt **83**. On the other hand, protonation of intermediate **81**

afforded thiazole **82** with better yield than that of compound **84**. Whatever the used molar ratio of allene **4a** and **80** was, the two substituted thiazoles (**82**[60] and **84**) came out with the same ratio.



Scheme 31

^{1}H NMR, ^{13}C NMR, IR, and high-resolution mass spectroscopy proved the structure of the new thiazole **84**. Like pyrazole **79**, hydrogen's assignment of thiophene ring of compounds **82** and **84** was carried out by comparing its ^{1}H NMR chemical shifts and coupling constants with the standard unsubstituted thiophene **85**[58] (Figure 6).

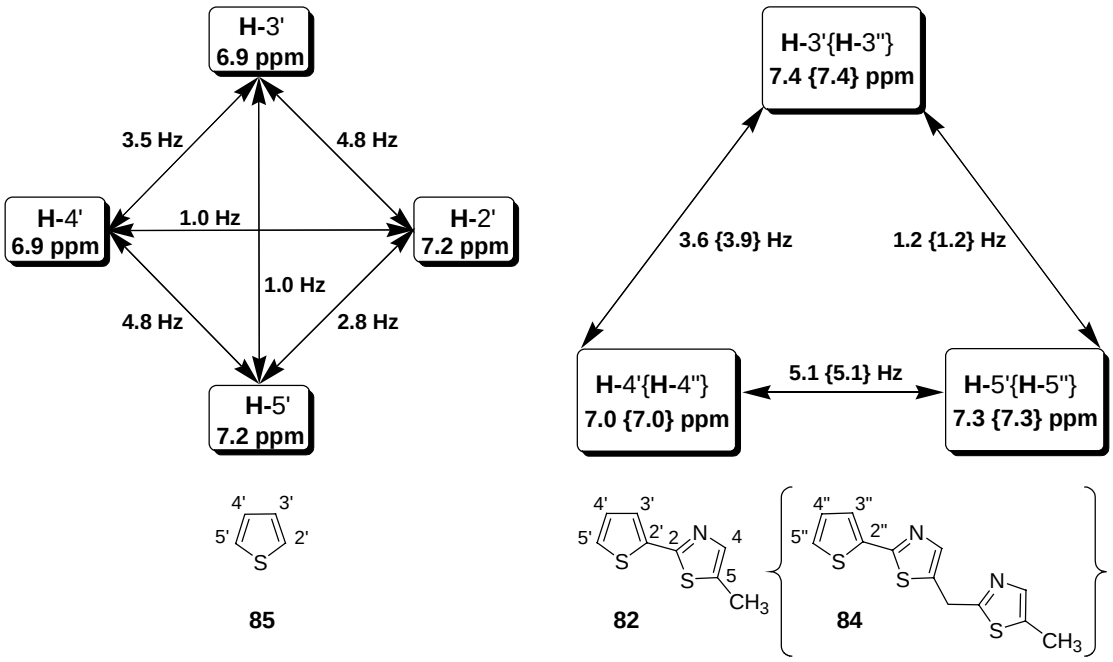


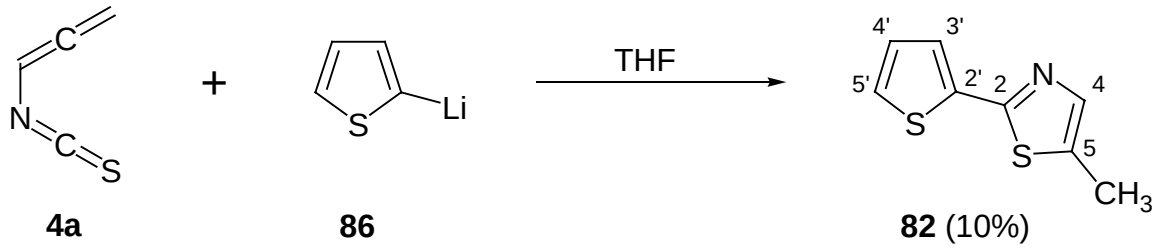
Figure 6

The clear downfield chemical shift of H-3' and H-3'' of compounds **83** and **84**, respectively, can be ascribed to the aromaticity of the formed thiazole ring at C-2' and C-2'' positions, respectively.

2.2.2.2.2 Reaction of Allenyl ITC 4a with Thienyllithium 86

Due to the electron-withdrawing inductive effect of the sulfur atom in the thiophene **85**, the C-2 position is more activated to deprotonation than the C-3 position in the presence of alkyl lithium reagent.[61]

Thienyllithium salt **86**[61] was easily prepared from reaction of *n*-butyllithium with thiophene by following a known procedure. The C–C bond formation was realized through the nucleophilic addition reaction of thienyllithium salt **86** to allene **4a** at –80 ºC in dry THF to result in 5-methyl-2-thiophen-2-yl-thiazole **82**[61] via electrocyclic ring closure with a 10% yield (Scheme 32).

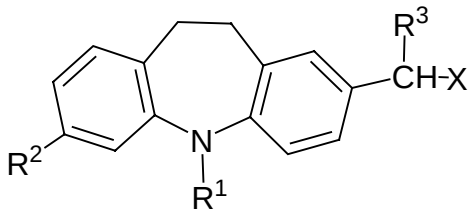


4a **86** **82** (10%)

Scheme 32

2.2.3 Reaction of Allenyl ITC 4a with 10,11-Dihydro-5*H*-dibenzo[b,f]azepine 88

The dibenzoazepine derivatives **87** have anti-inflammatory, analgesic, and antipyretic activity in addition to their ability to absorb the irritating rays of ultraviolet light (Scheme 33).[62] Studying the nucleophilicity of the secondary aromatic amine **88** toward allene **4a** was not the only target of this point, but also the C–N bond formation and synthesis of a new substituted thiazole (Scheme 34).

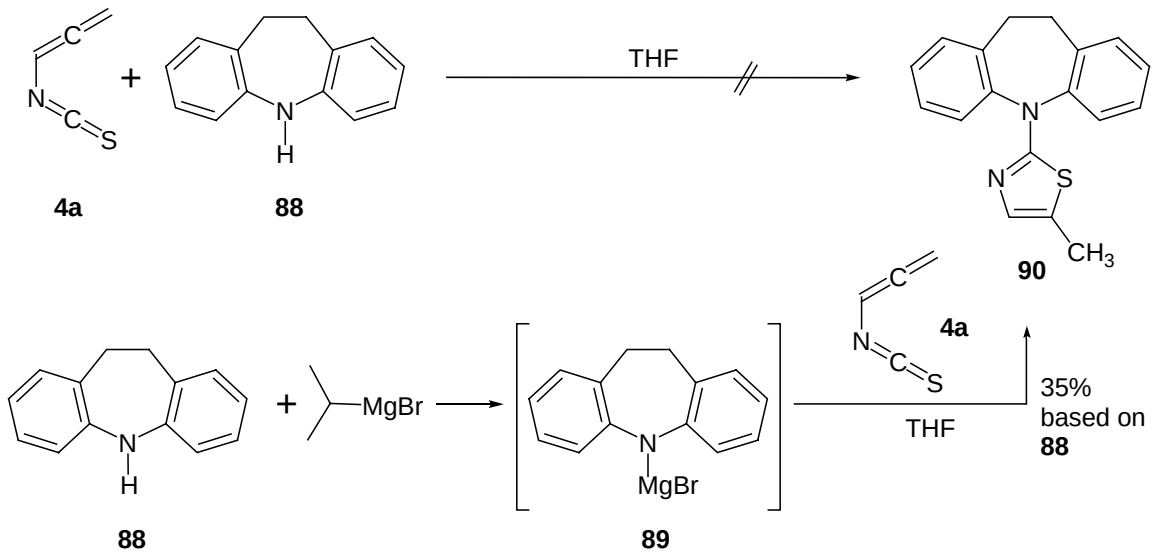


R^1 = H, alky, or benzyl
R^2 = H or halogen
R^3 = H or alkyl
X = COOH, CN, or COOR (R = alkyl)

87

Scheme 33

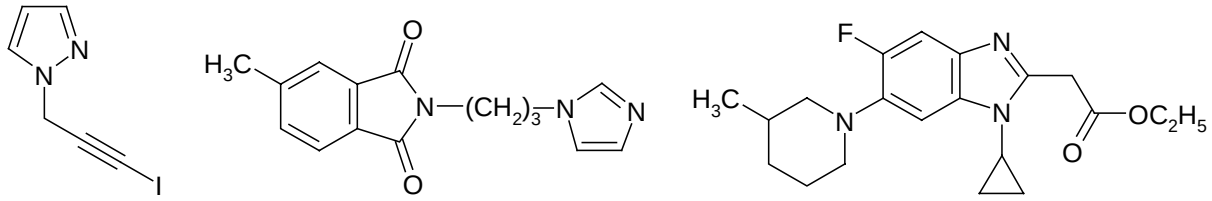
The C–N bond association was performed via the reaction of allene **4a** with dibenzoazepinylmagnesium bromide **89**, which was prepared by reacting the amine **88** with isopropylmagnesium bromide in dry THF, to generate the newly substituted thiazole **90** (35% yield), see Scheme 34. It is important to mention that the ITC **4a** did not react with dibenzoazepine **88** even after several days at room temperature. This can be attributed to the poor availability of the lone pair of amine bearing two aromatic substituents causing a strong decrease of the nucleophilicity of the nitrogen atom.



Scheme 34

2.2.4 Reaction of Allenyl ITCs 4a and 21 with Heterocycles Containing Two Nitrogen Atoms

Many of azole (pyrazole, imidazole and benzimidazole) derivatives exhibit remarkable biological activities[9,63–69] such as substituted pyrazole **91** (as antifungal),[9] imidazole **92** (as antihypertensive),[66] and benzimidazole **93** (as antimicrobial and antifungal), see Scheme 35.[68]



91 **92** **93**

Scheme 35

On the basis of their biological importance and high reactivity, the vision of our research became to probe the N–C bond formation and the regioselectivity of different azole compounds (as nucleophiles) as well as to synthesize novel substituted heterocycles.

A new family of substituted thiazole derivatives carrying different heterocyclic ring systems at C-2 position was prepared via the reaction of the allenyl ITCs **4a** and **21** with the substituted pyrazoles **94a–c**, imidazoles **95a**,**b**, and benzimidazole **96** (Table 7).

In some reactions we obtained two isomers, the aromatic substituted thiazole and the nonaromatic substituted thiazole, while in other reactions we got only one major aromatic substituted thiazole.

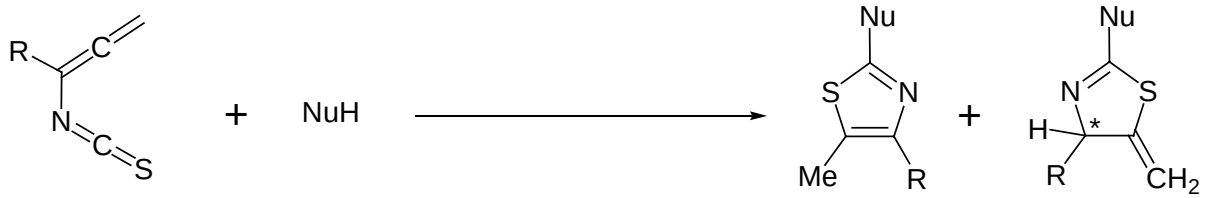
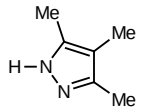
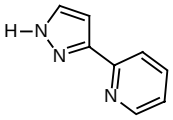
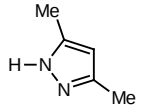
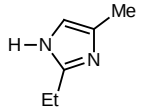
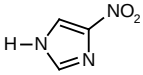
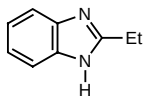
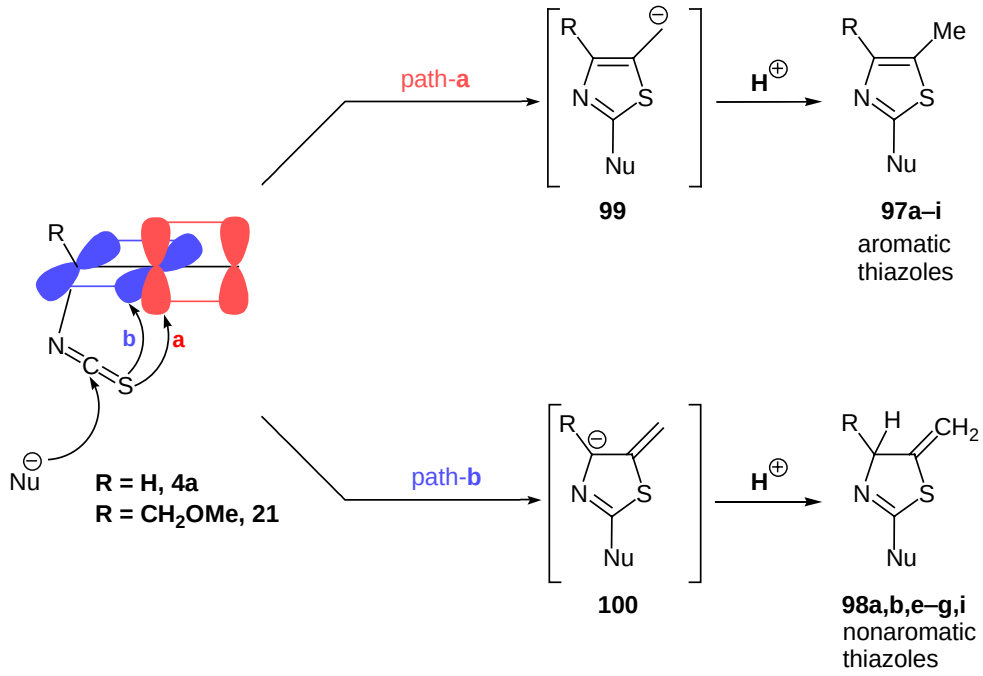


Table 7

	Nucleophile	Electrophile	Solvent	Reaction Time	Aromatic thiazole 97	Yield (%)	Nonaromatic thiazole 98	Yield (%)
		**4a**	CH_2Cl_2	2 h	**a**	66	**a**	22
	a[70]	**21**	CH_2Cl_2	5 h	**b**	39	**b**	46
94		**4a**	$CHCl_3$	24 h	**c**	91	----	----
	b[71]	**21**	$CHCl_3$	24 h	**d**	88	----	----
		**4a**	CH_2Cl_2	3 h	**e**	49	**e**	33
	c	**21**	CH_2Cl_2	6 h	**f**	50	**f**	30
								
95	**a**	**21**	THF	1 h	**g**	79	**g**	3
								
	b	**4a**	DMF	5 days	**h**	68	----	----
96								
		21	THF	40 h	**i**	76	**i**	17

This dichotomy of behavior for the formation of the aromatic substituted thiazoles **97a–i** and nonaromatic substituted thiazole rings **98a**,**b**,**e–g**,**i** may be explained as shown in Scheme 36. Generally, the formation of these thiazoles was performed via the nucleophilic attack of sulfur at one of the two perpendicular π-bonds. The nucleophilic attack at the terminal π-bond (red-colored, path-**a**) revealed the carbanion **99**. Protonation of the intermediate **99** afforded the

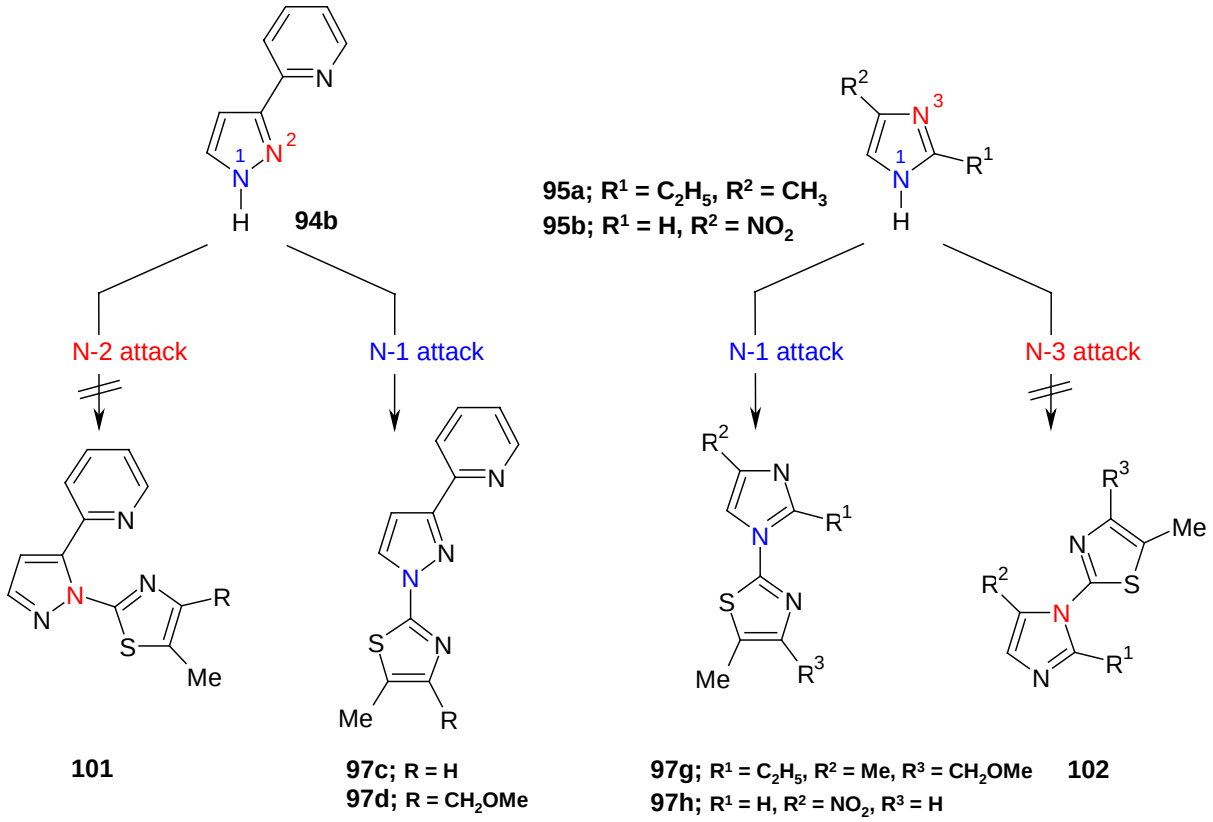
aromatic substituted thiazoles **97a–i**. On the other hand, the nucleophilic attack at the inner π-bond (blue-colored, path-**b**) led to the formation of the intermediate **100**, which upon protonation yielded the nonaromatic heterocycles **98a**,**b**,**e–g**,**i**, if this reaction is so rapid, that equilibration of **99** and **100** is excluded. Formation of **100** may be advantageous for geometrical reasons leading to the product of kinetically control. Obviously, compounds of type **97** are the thermodynamically favored product.



Scheme 36

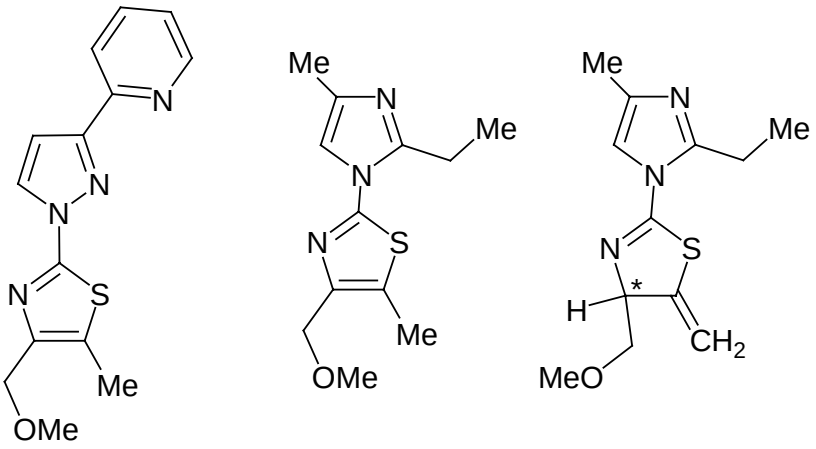
Although the nonaromatic thiazoles **98a**,**b**,**e–g**,**i** are stable at –18 °C for several months, they can be converted quantitatively into the preferential more stable aromatic forms **97a–i** in the presence of $CDCl_3$ (Table 7). The rate of conversion was found to be concentration dependant. Further details for each reaction are shown in Table 7.

The reaction of reactants **94b** and **95a**,**b** with allenyl ITCs **4a** and **21** yielded compounds **97c**, **97d**, **97g**, and **97h** (Table 7). For these reactions, there were two possible nucleophilic centers; either from the assigned nitrogen N-1, nitrogen N-2, or nitrogen N-3. A presentation of the possible regiochemistry for such compounds is shown in Scheme 37.



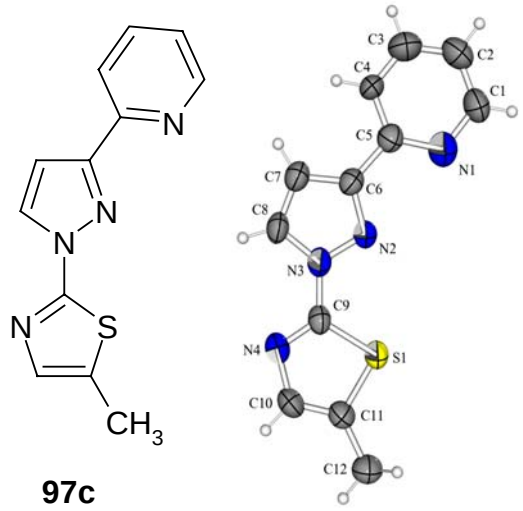
Scheme 37

The nucleophilicity of reactants **94b**, **95a** was most probably raised from the less sterically hindered nitrogen (N-1 of reactants **94b** and **95a**). Thus, the expected chemical structure of compounds **97c**, **97d**, **97g**, and **98g** was similar to the drawn structure in Scheme 38. Fortunately, a sample of compound **97c** was obtained in crystalline form and could be subjected to a diffraction analysis as shown in Figure 7. This compound was a result as might be predicted from steric considerations. The regiochemistry of compound **97d** would be similar to that of thiazole **97c**. Unfortunately, we could neither do X-ray analysis of substituted thiazoles **97g** and **98g** since their physical state was oily nor find a similar example in the literature to compare their chemical shifts and values of the imidazole's protons.



97d **97g** **98g**

Scheme 38



97c

Figure 7 ORTEP drawing of compound **97c**

The critical factor for the nucleophilicity of the reactant **95b** (Table 7) may be mainly controlled by the electronic effect of the nitro group, which can affect the nucleophilicity of the both nitrogen atoms. Fortunately, the obtained X-ray crystal structure of thiazole **97h** provided the opportunity to assign its absolute regiochemistry (Figure 8). Thus, N-1 was the more nucleophilic center for attacking allene **4a** to afford only compound **97h** with 68% yield.

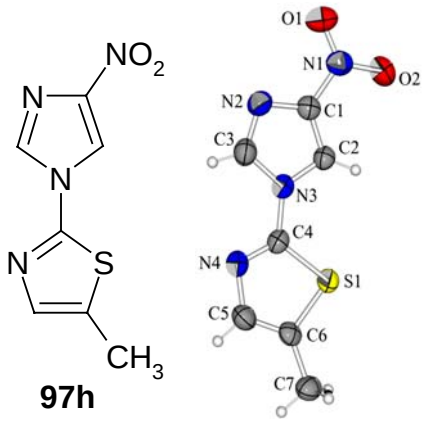
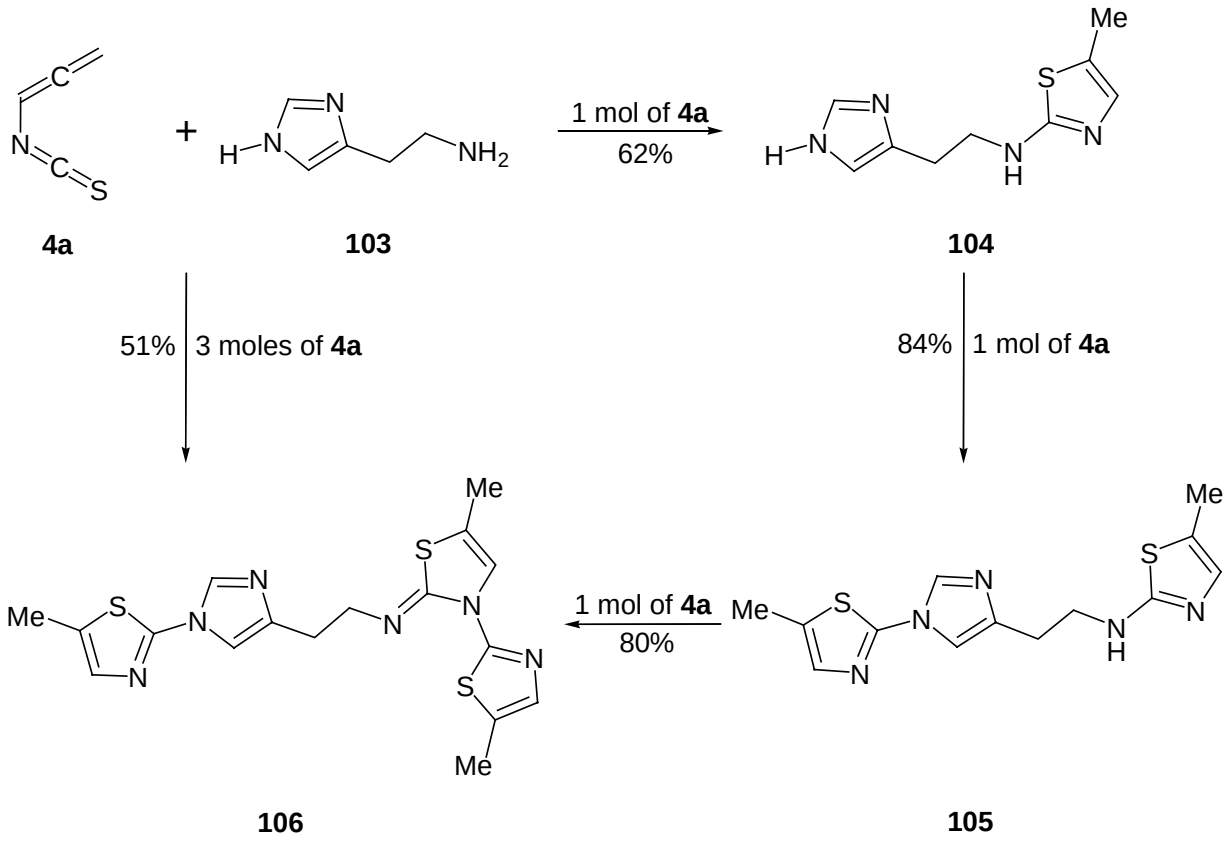


Figure 8 ORTEP drawing of compound **97h**

2.2.5 Reaction of Allenyl ITC 4a with Histamine 103

Histamine **103** is a naturally occurring compound, which is an important mediator of inflammation and gastric acid secretion (Scheme 39).[72] It has two interesting nucleophilic centers, the imidazole ring and the primary amino group. For these reasons, it was important to study the regioselectivity (reactivity) of the two nucleophilic centers and the stereochemistry of the resulting product.

To investigate the reactivity of the histamine **103**, it was treated step by step with a threefold molar excess of allene **4a**. Depending on the ^{1}H NMR chemical shift of the starting material **103** in CD_3OD as a reference, we noticed a clear downfield chemical shift for the four protons on the ethyl chain (2.86 and 3.47 ppm) of compound **104**, while they appeared in the starting material **103** in CD_3OD at 2.71 and 2.85 ppm. These chemical shifts of compound **104** were caused by the formation of the thiazole ring on the amino group. The nucleophilicity of the primary amine group was stronger than that of the imidazole moiety. Additionally, the IR spectrum of thiazole **104** revealed two typical amino bands at 3447 (NH of the imidazole ring) and 3218 cm^{-1} (NH of the secondary amine). Since the absorption bands of the primary amine (NH_2) and imidazole moiety of the starting material **103** appeared as a broad band (2700–3500 cm^{-1}), it was impossible to include them in comparison studies of IR results for this reaction.



Scheme 39

On the basis of the ^{1}H NMR spectrum, the chemical shifts of the imidazole's protons **105** (7.46 and 8.22 ppm in CD_3OD), which had been shifted downfield in comparison to the starting material's protons **104** (6.84 and 7.57 ppm in CD_3OD), proved clearly the formation of thiazole ring on the imidazole moiety. On the other hand, the four protons of the ethyl chain of compound **105** revealed only a small difference in their ^{1}H NMR chemical shifts compared to heterocycle **104**.

Moreover, the absence of the absorption band at 3447 cm^{-1} (NH of the imidazole moiety) and the presence of the characteristic absorption band at 3195 cm^{-1} (NH of the secondary aromatic amine), in comparison with the IR spectrum of thiazole **104**, were additional proofs of the expected structure of histamine derivative **105**. The nucleophilic attack occurred from the imidazole moiety rather than the secondary aromatic amine due to the steric factor and the low nucleophilicity of this amine. Finally, treating compound **105** with one mole of allene **4a** ended with the formation of **106** with a yield of 80%. Additionally, treating histamine **103** with 3 moles of allene **4a** (as one-pot reaction) afforded substituted thiazole **106** with a 51%

yield. The regiochemistry and the stereochemistry [of the imine group N(4)=C(10)] of compound **106** were detailed by the X-ray study (Figure 9).

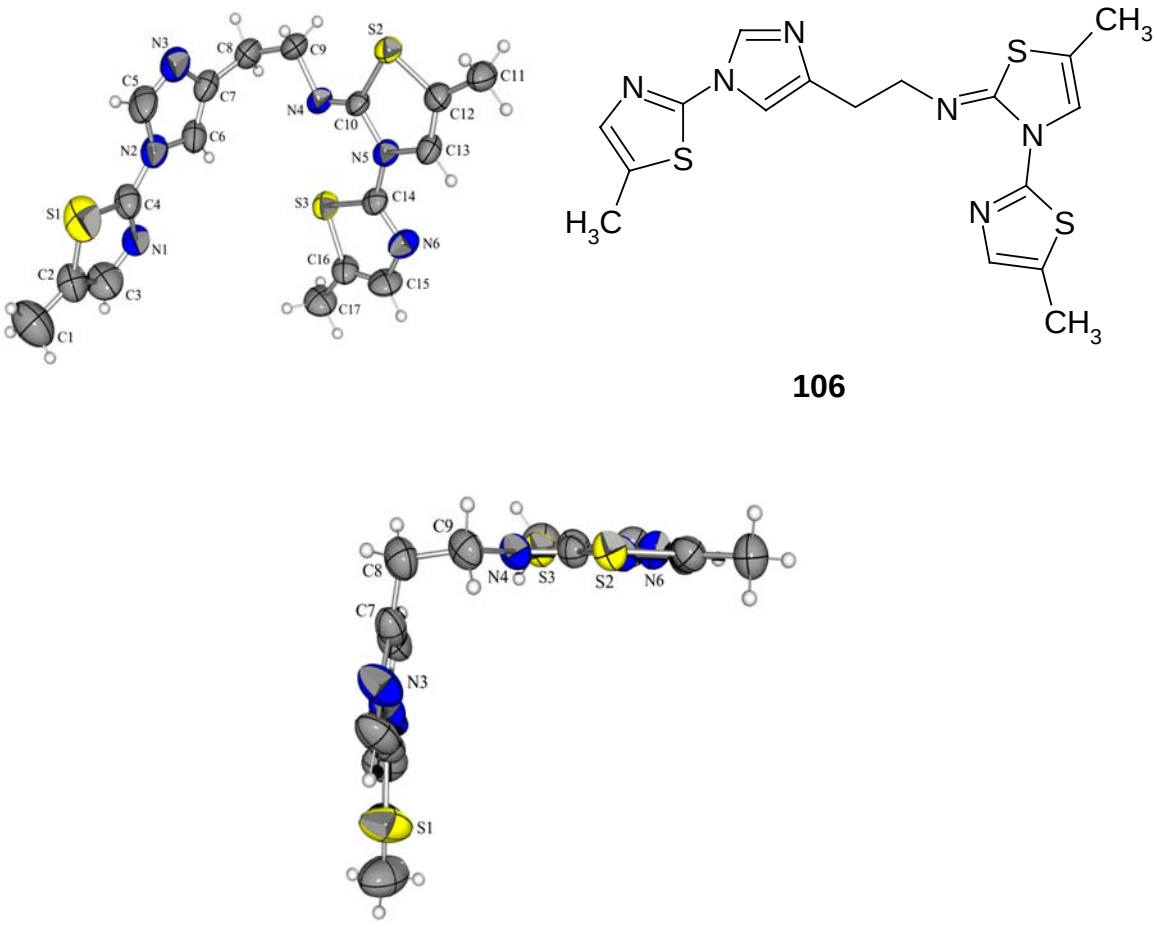
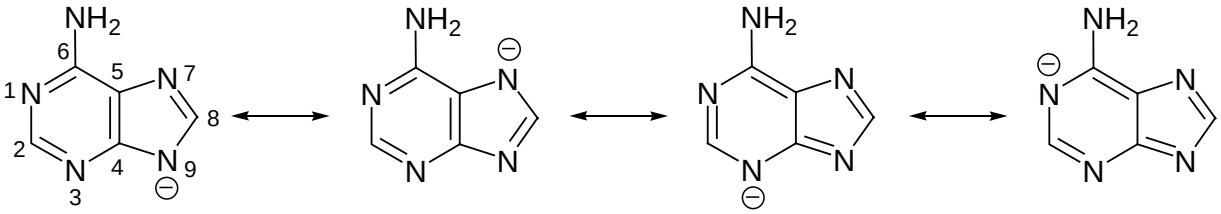


Figure 9 ORTEP draw of histamine **105**

Obviously, the thiazole ring was formed at the less sterically hindered nitrogen of the imidazole moiety. The stereochemistry of the imine group was found to exhibit (*Z*) configuration.

2.2.6 Reaction of Allenyl ITC 4a with Adenine 107

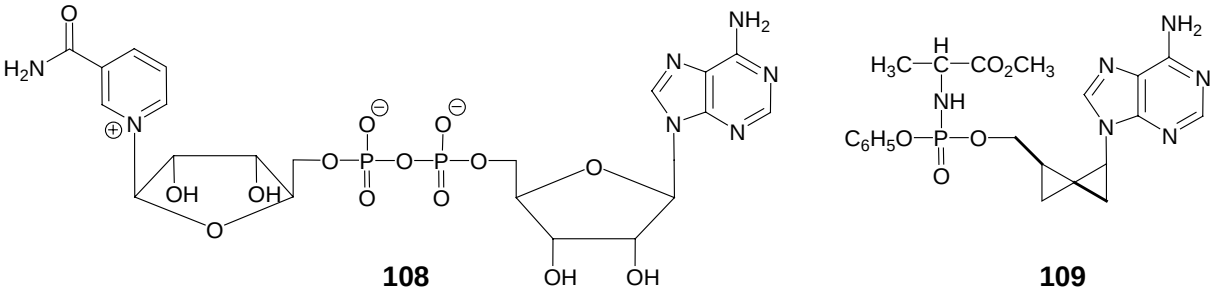
9*H*-Purin-6-ylamine (adenine) **107** exists in many biological systems and it is an important derivative of purine, which is a basic part of the RNA and DNA (Scheme 40).[73]



107a **107b** **107c** **107d**

Scheme 40

Adenine **107** is present in one of the most important coenzymes in biological oxidations, the nicotinamide adenine dinucleotide **108** (NAD^+, the oxidized form and NADH is the reduced form, Scheme 41). Additionally, adenine derivatives have widespread application in drugs such as compound **109**, which has high activity against human cytomegalovirus.[74]



108 **109**

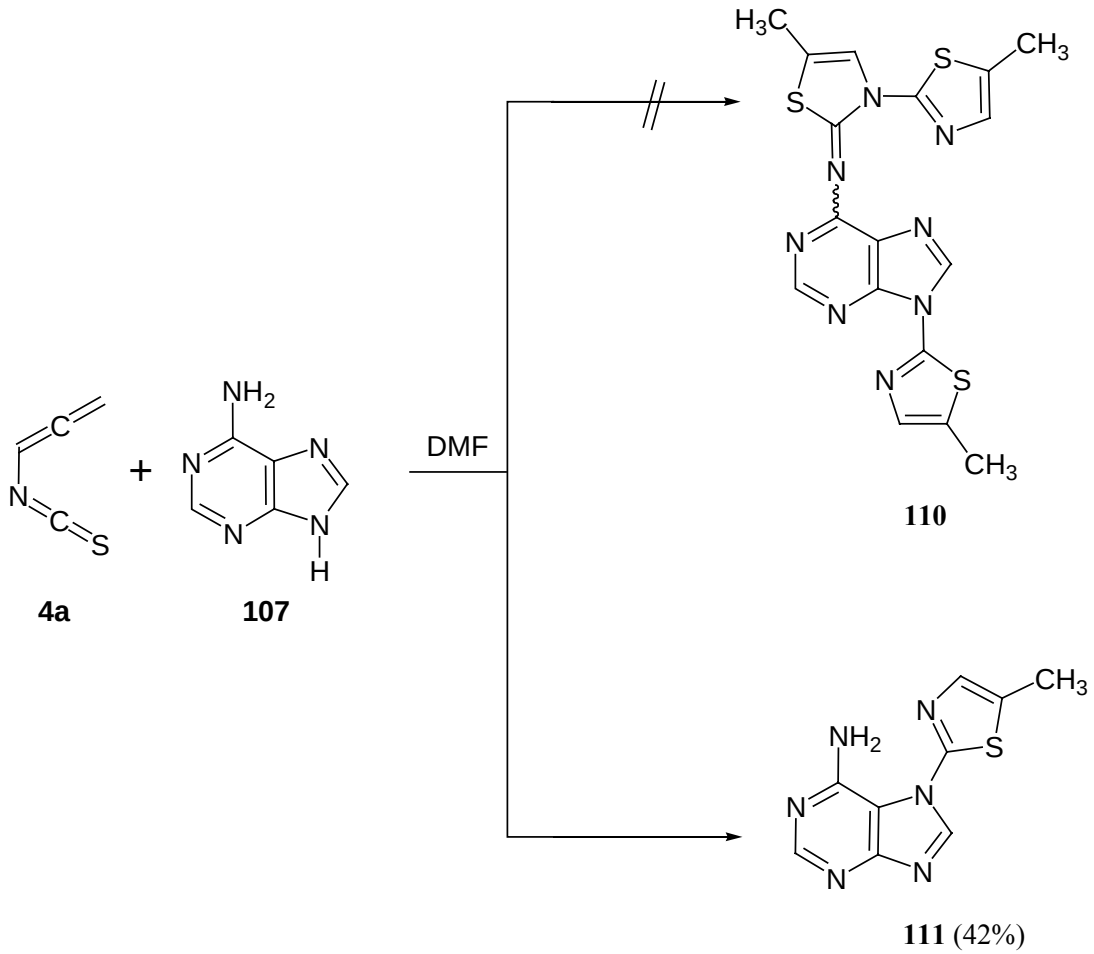
Scheme 41

The stability order for N-substituted adenine **107** was indicated by tautomeric equilibria studies,[75] alkyl rearrangement reactions,[76] and self-consistent field (SCF) molecular orbital calculations[77] to be N-9 ≥ N-7 ≥ N-3 > N-1 with gaps of 2–10, 85–210, and about 25 kJ/mol, respectively.

Moreover, the determining factor for the relative rates of reaction of heterocyclic nitrogen is governed by the steric factor.[78a] Although the nucleophilicity at N-9[78a–c] is usually dominant, there have been many reports of minor attack (nucleophilicity) by N-3[79] and/or N-7.[80]

Adenine **107** was treated with excess amount of the allenyl ITC **4a** in order to investigate the reactivity of the N-1, N-3, N-7, N-9 and the primary aromatic amine (NH_2), see Scheme 40. Our speculation for the resulting product was the polysubstituted adenine **110**. Surprisingly, we got only a mono-substituted adenine **111** at the more sterically hindered and less nucleophilic nitrogen, N-7 with 42% yield, as shown in Scheme 42.

The IR spectrum of thiazole **111** showed only the absorption band of the primary aromatic amino group (NH_2) at 3254 cm^{-1}.



Scheme 42

The regiochemistry of the found product as well as the hydrogen bond association were confirmed by the X-ray study as shown in Figure 10. This abnormal formation could be explained due to the intramolecular hydrogen bonding association between the 6-amino group (N-10 or N-11) and the nitrogen atom (N-10′or N-11′) in the thiazole ring.

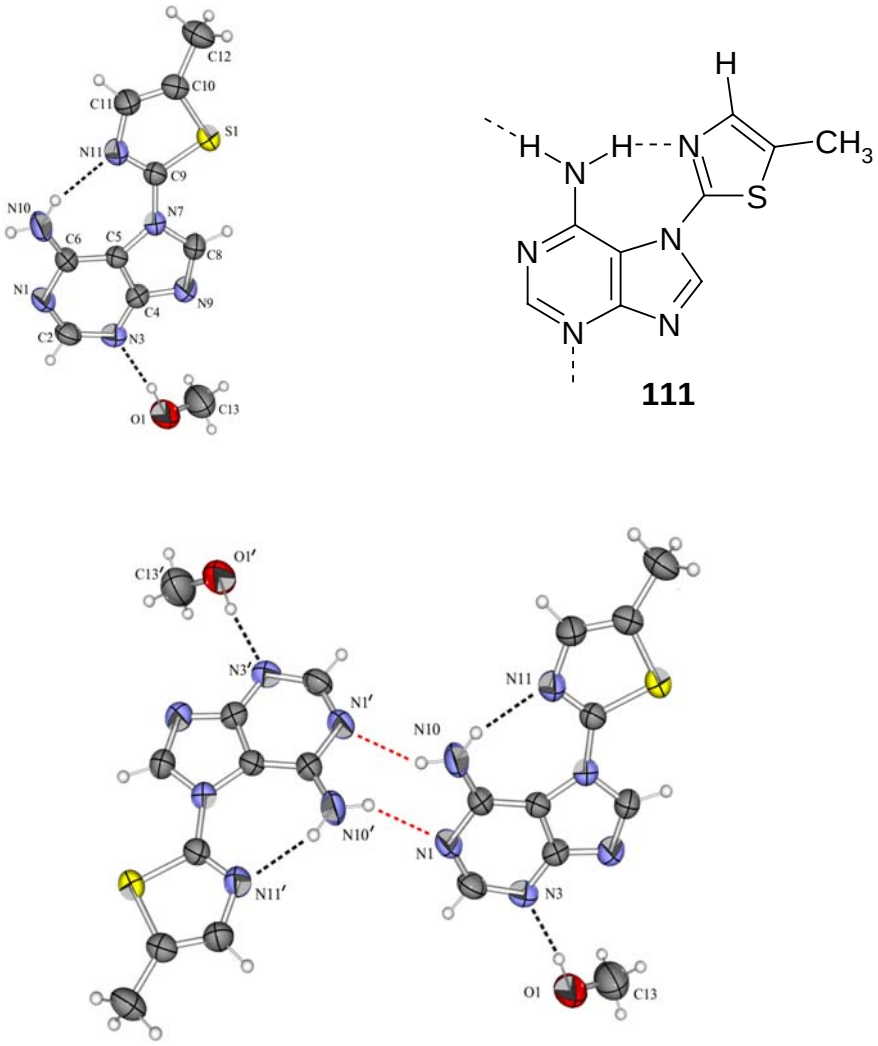


Figure 10 ORTEP draw of adenine **111**

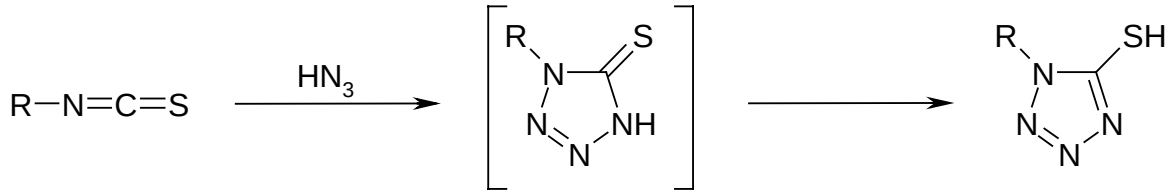
The crystal formation of adenine derivative **111** was obtained from methanol at 25 °C as beige plates. For this reason the methanol molecule appeared in the X-ray measurement, whereas methanol made intermolecular hydrogen bonding with N-3 of adenine **111**. These crystals were monoclinic, P2(1)/n, and contain 4 molecules within the unit cell.

Moreover, the intramolecular hydrogen bonding distance of {N(10)–H---N(11)} was found to be 279.0(6) pm {N, N distance}, which is representing a strong hydrogen bond interaction according to Emsley et al.[81] On the other hand, the intermolecular hydrogen bonding distance of {N(10)–H---N(1´)} and {O(1)–H---N(3)} was obtained as 304.1(6) and 280.8(5) pm, respectively, which represent weaker hydrogen bonding interaction than that of the {N(10)–H---N(11)} case. Nevertheless, the hydrogen bond strength of {O(1)–H---N(3)} interaction was close to the hydrogen bond association of {N(10)–H---N(11)} case.

2.3 Advanced Succeeding Reactions of Allenyl ITC 4a: Synthesis of Bifunctional Thiazoles

2.3.1 Reaction of Allenyl ITC 4a with Hydrazoic Acid

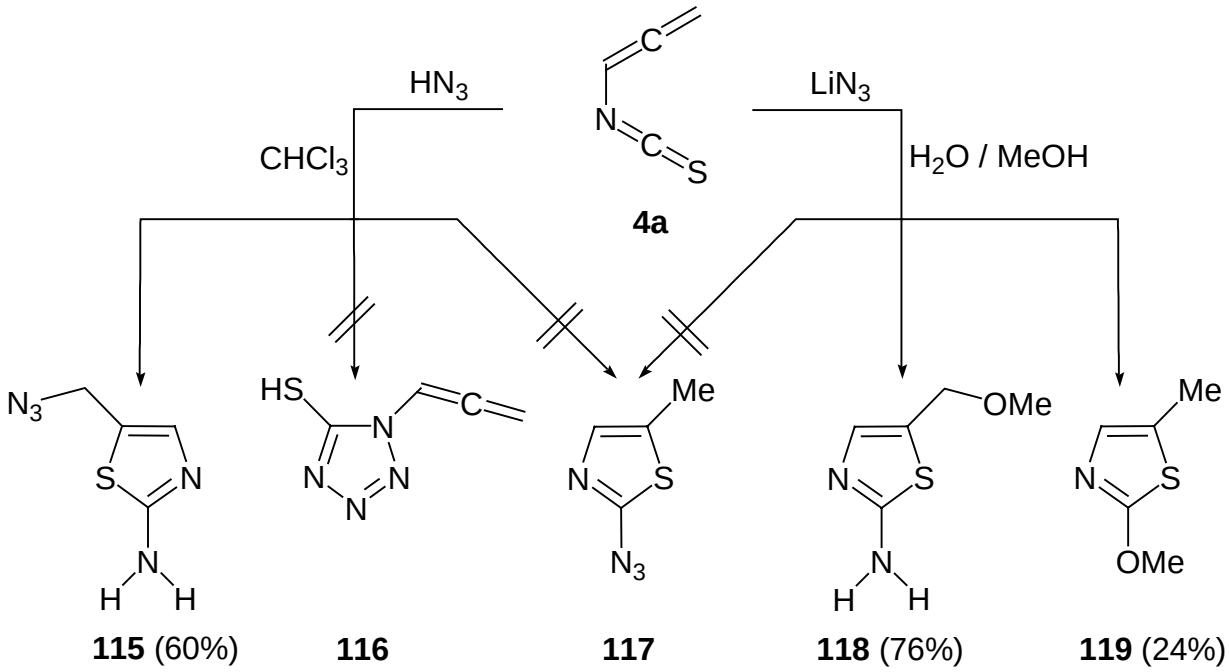
The reaction of the ITC derivatives **112** with the hydrogen azide was reported by Huisgen[82] in 1963. This reaction led to the formation of substituted 5-mercapto-tetrazole derivatives **114** due to the dipolar cycloaddition of 1,3-dipoles (i.e. azide) to a dipolarophile (i.e the C=N bond of the isothiocyanate group in **112**, Scheme 43).



112 **113** **114**

Scheme 43

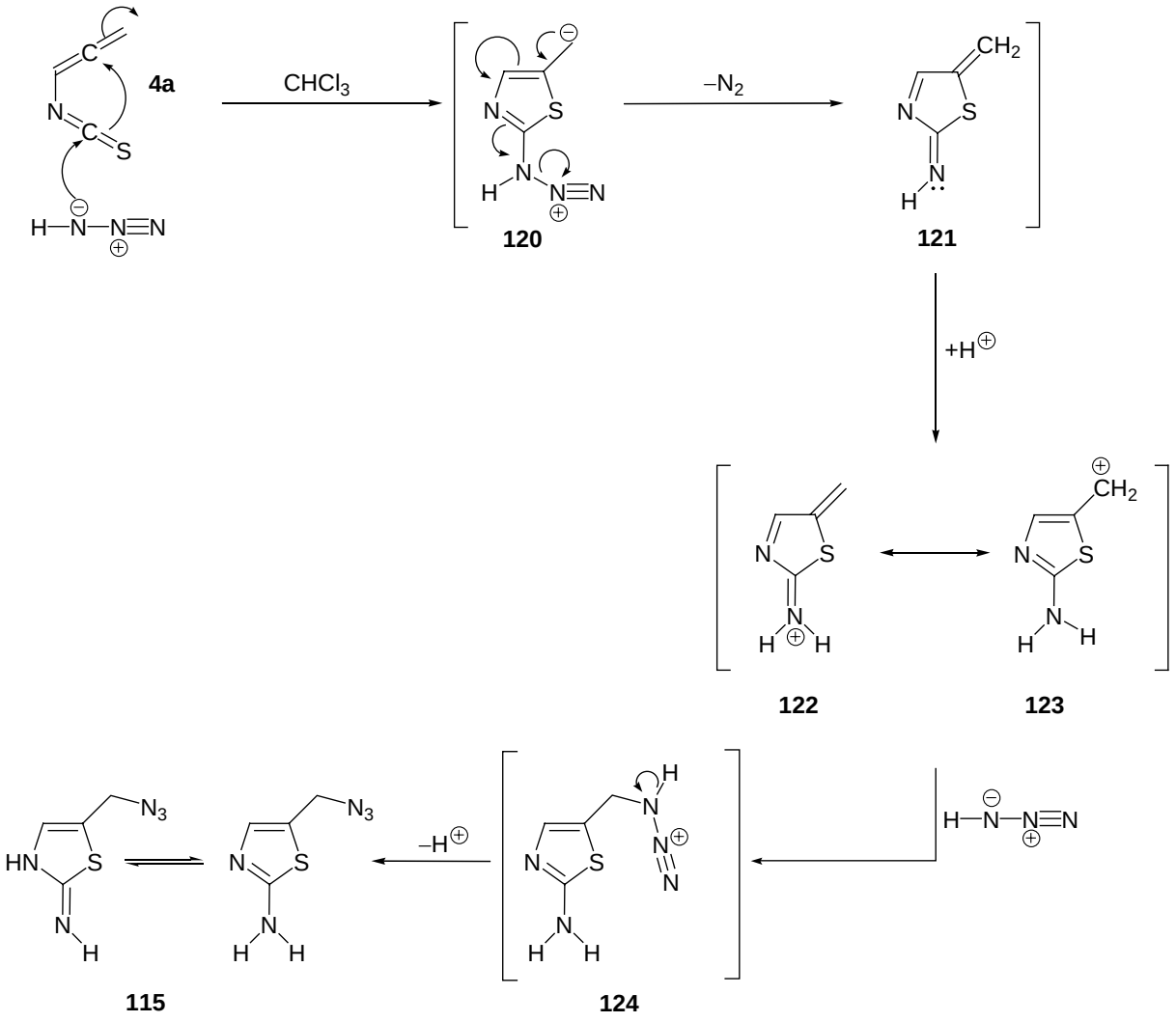
In contrast, the reaction of allenyl ITC **4a** with an excess of hydrazoic acid[83] in chloroform afforded, after two days at room temperature, 5-azidomethyl-thiazol-2-ylamine **115** in 60% yield, while neither the tetrazole **116** nor trivial substituted thiazole **117** were formed (Scheme 44). Also in the case of the reaction of ITC **4a** with LiN_3 in a protic solvent (methanol) not the expected heterocycle **117** was obtained but rather mainly thiazole **118**.[8b]



Scheme 44

Obviously, the formation of the thiazole **115**, as a result of electrocyclic ring closure via the sulfur attack on the terminal allenic π-bond, was faster than that of the formation of the normal substituted tetrazole-thiol **116**.

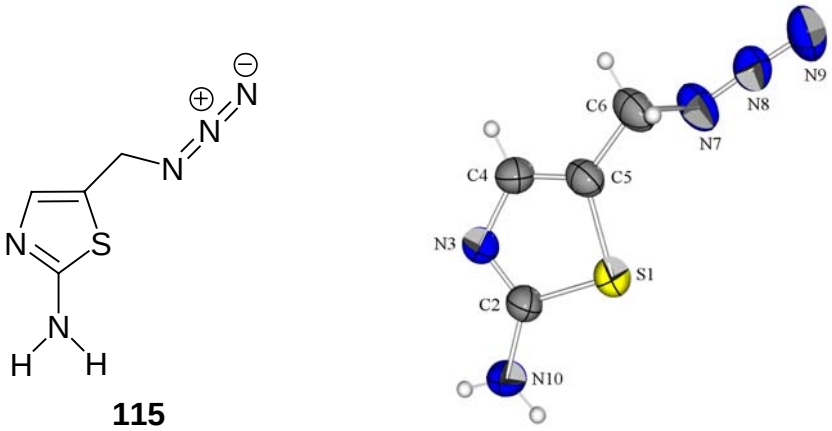
The reaction mechanism of the obtained nontrivial thiazole **115** may be detailed as shown in Scheme 45. The cleavage of intermediate **120** resulted in imine **121**. Protonation of the later intermediate revealed the resonance-stabilized cations **122** ↔ **123**. Preferential attack of the carbonium ion **123** by another molecule of HN_3 afforded the intermediate **124**, which gave the bifunctional thiazole **115** on deprotonation.



Scheme 45

The IR spectrum of thiazole **115** showed two typical absorption bands at ~ 3410 (NH_2) and 2101 (N_3) cm^{-1}, while the ^{13}C NMR spectrum revealed a clear downfield chemical shift of the methylene carbon C-1' at 47.1 ppm. This could be ascribed to the electronic effect of the azido group.

However, the structure of the bifunctional thiazole **115** was proved by physical methods and elemental analysis in addition to the X-ray crystallographic measurement (Figure11).



115

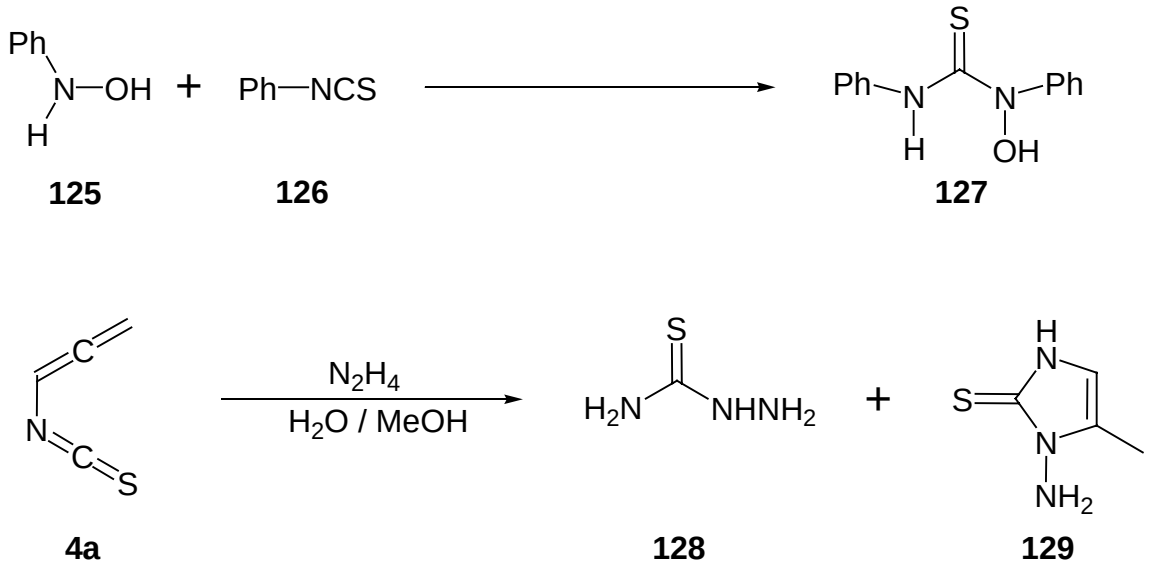
Figure 11 The ORTEP drawing of thiazole **115**

Yellow needles of azido **115** were obtained by diffusion-controlled addition of *n*-hexane into a dichloromethane solution containing **115** at 25 °C. These needles are monoclinic, space group P2(1)/c, and contain four molecules within the unit cell.

The azide functional group is close to linear [N(7)–N(8)–N(9) = 173.6(4)°] and the C(6)–N(7)–N(8) angle is 114.5(3)°. Moreover, the shorter terminal N(8)–N(9) bond is 113.1(4) pm and the bond distance N(7)–N(8) is 122.6(4) pm. The obtained bond lengths of C(2)–N(3), S(1)–C(2), and C(2)–N(10) was found to be 130.6(4), 174.2(3), and 134.1(4) pm, respectively. Further, the hybridization at the carbon C(2) was found to be sp^2-type [the sum of angles 360.0(5)°]. These results are consistent with the published data of compounds with a similar structure.[84]

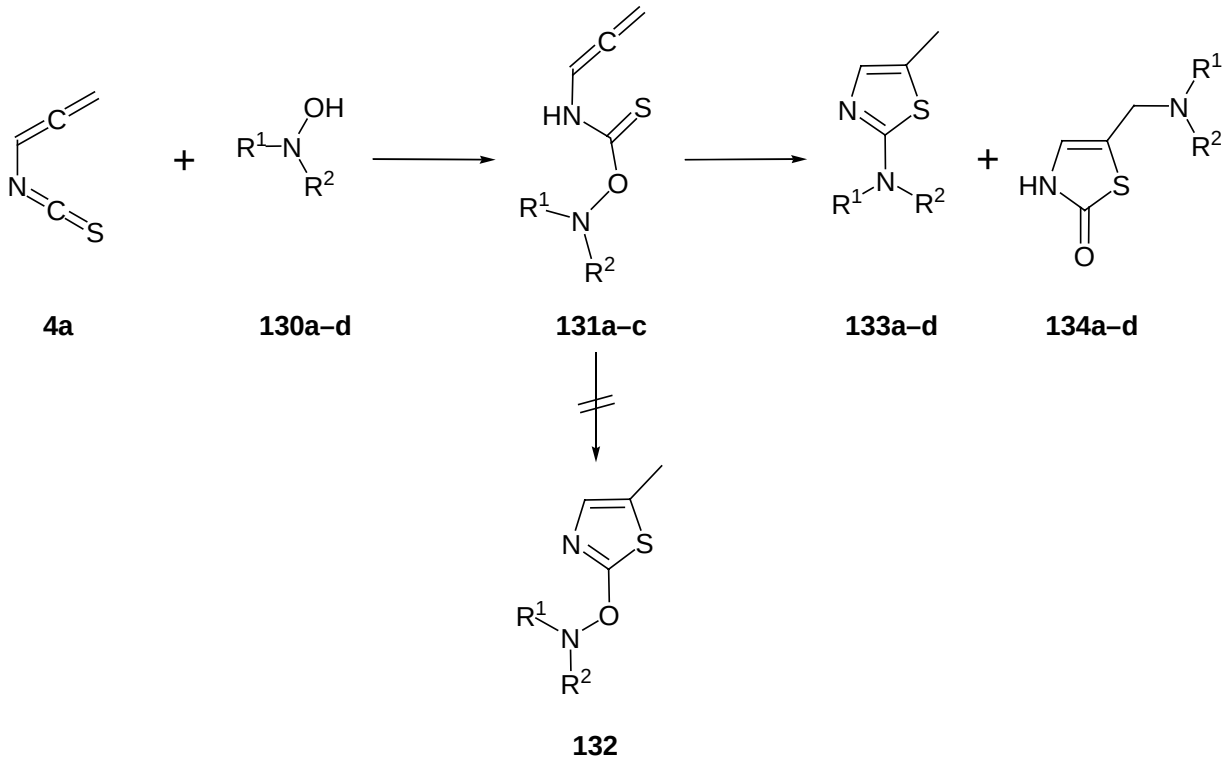
2.3.2 Reaction of Allenyl ITC 4a with *N,N*-Disubstituted Hydroxylamine Derivatives

B. Hirsch[85] reported the reaction between the hydroxylamine derivative **125** and the phenyl isothiocyanate derivative **126**, which afforded the thiourea derivative **127** (Scheme 46). Moreover, K. Banert[8a] reported the reaction of allene **4a** with hydrazine, which has weak N–N covalent bond, in the presence of a protic solvent mixture of (H_2O/MeOH) to result in the thiosemicarbazide **128** and imidazole derivative **129**.



Scheme 46

For these reasons it was interesting and important to investigate the chemistry of hydroxylamine derivatives **130a–d** toward our basic allene **4a** (Scheme 47). One of the investigated compounds exists as a hydrochloride salt **130d** and the other three **130a–c** are available as free bases.



4a **130a–d** **131a–c** **133a–d** **134a–d**

132

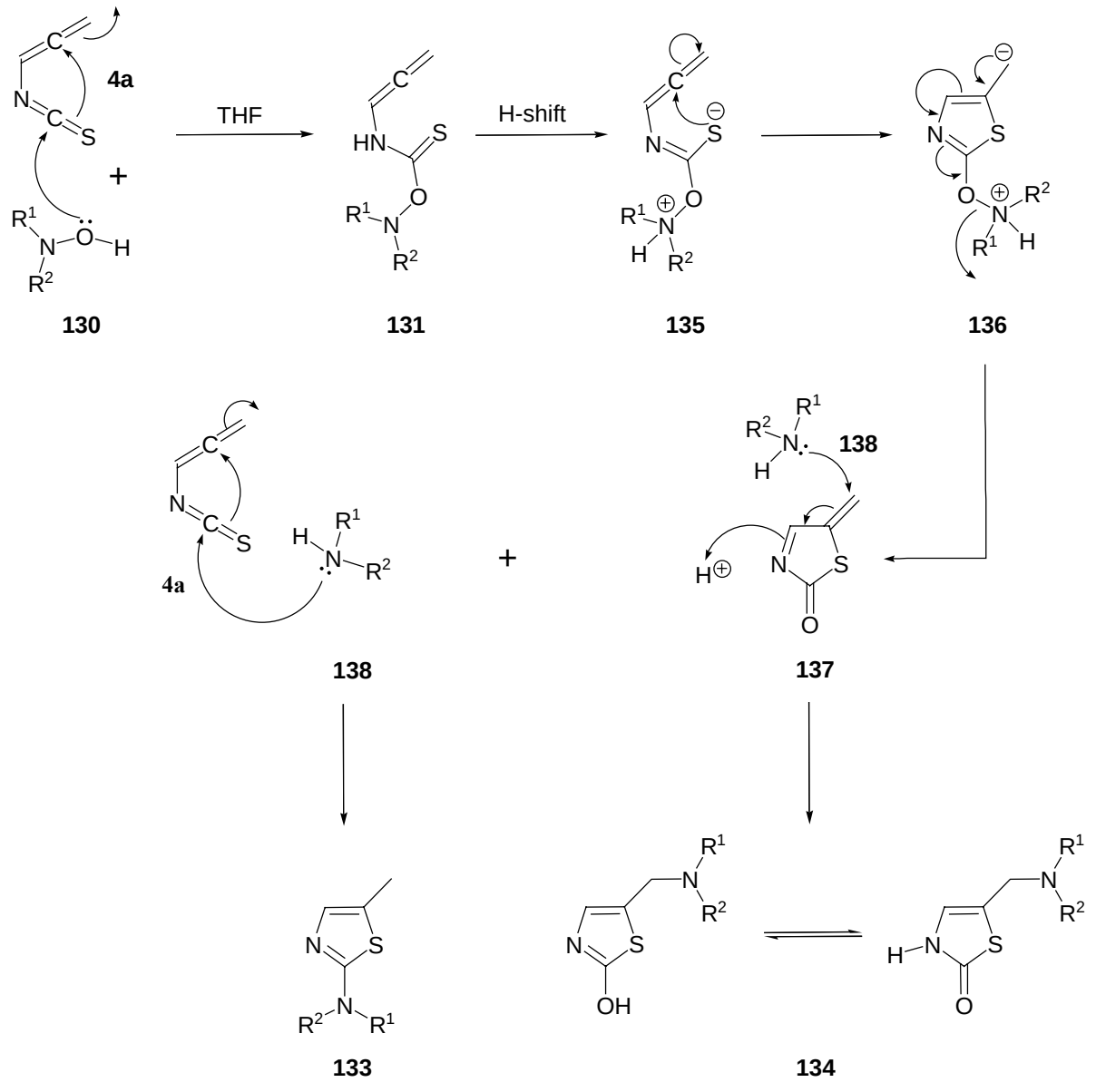
	R^1	R^2	^{1}H NMR Yield (%)	^{1}H NMR Yield (%)	Isolated Yield (%)	
			131[a]	**134**[a]	**133**[b]	**134**[b]
a	Et	Et	86	60	29	55
b	–$(CH_2)_5$–		83	51	30	40
c	CH_2Ph	CH_2Ph	80	61	33	35
d	Me	Me	----[c]	----[c]	49	----[c]

[a]Excess amount of hydroxylamine was used. Experiments were carried out in $CDCl_3$ and grease was used as a reference for calculating the yield.
[b]Excess amount of allene **4a** was used.
[c]Hydrochloride salt. For compound **130d**, the salt was transferred into free hydroxylamine only in a solution mixture of THF/H_2O in the presence of a base. For this, the NMR-tube experiment could not be excecuted.

Scheme 47

Treating hydroxylamines **130a–d** with ITC **4a** did not generate the trivial thiazoles **132** but afforded two products, heterocycles **133a–d** and compounds **134a–c**. The formation mechanism of these unexpected products (**133a–d** and **134a–c**) is shown in Scheme 48. The nucleophilic addition of the hydroxylamines **130** to the ITC **4a** led to the formation of the unstable thiourethane compounds **131**, which cyclized after proton shift to give **136**. Cleavage

of intermediates **136** liberates the amine **138** (Scheme 48). Thiazoles **133** were formed by the nucleophilic attack of the liberated amine **138** to the excess amount of the basic allene **4a** via trivial ring closure. Nucleophilic addition of secondary amines **138** to the terminal double bond of intermediate thiazole derivative **137** afforded bifunctional thiazoles **134**.



The terms R^1 and R^2 are explained in Scheme **47**.

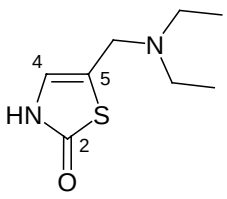
Scheme 48

However, reacting allene **4a** with an excess amount of compounds **130a–c** in $CDCl_3$ led to the formation of intermediates **131a–c** within 13–17 min, respectively. These intermediates **131a–c** were rearranged to furnish one major product, thiazoles **134a–c** (Scheme 47). Moreover, the isolated intermediates **131a–c** were unstable on silica gel and underwent further rearrangement to offer bifunctional thiazoles **134a–c** (Scheme 47).

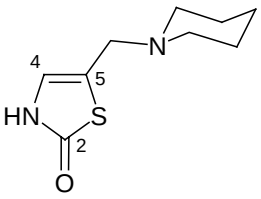
Thiazole **133a** was reported in the literature,[86] and the structure determination in our work was supported by ^1H and ^{13}C NMR, IR, and GC–MS. The ^1H NMR spectrum showed a clear downfield chemical shift of the methylene protons within the ethyl groups of **133a**[86] (3.41 ppm, in $CDCl_3$) in comparison to the starting material **130a** (2.66 ppm, in $CDCl_3$), due to the aromaticity of the thiazole ring. On the other hand, the ^1H NMR chemical shift of the aliphatic methylene protons within the ethyl groups of compound **134a** was at 2.55 ppm ($CDCl_3$), which was quite similar to the chemical shift of the aliphatic starting material **130a** (2.66 ppm, in $CDCl_3$).

However, the structure of product **134a–c** was assigned based on the ^1H, ^{13}C, ^{15}N NMR spectra (**134a**), ^{13}C ^1H correlation spectroscopy (**134a**), and ^1H NMR NOE difference spectra (**134a**, **134b**), IR spectra, elementary analyses (**134a**, **134b**), high-resolution mass spectra (**133a**, **134c**) and X-ray diffraction (**134b**).

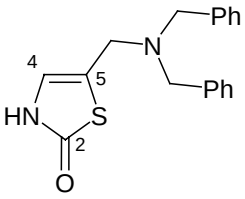
The ^{13}C NMR showed characteristic signals at 176 ppm (C=O) and between 117–120 ppm (=CH, C-4), while the infrared absorption showed two characteristic absorption bands at about 3155 cm^{-1} (NH) and about 1655 cm^{-1} (C=O), which were consistent with data of the known model compound **139**[87] (Table 8).



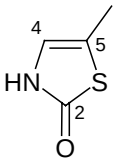
134a



134b



134c



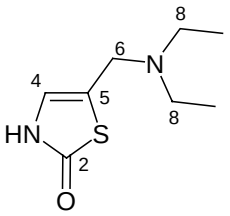
139

Table 8

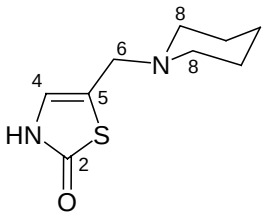
	Compound 134a		Compound 134b		Compound 134c		Compound 139	
Assigned atoms	**^{13}C NMR**	**IR**	**^{13}C NMR**	**IR**	**^{13}C NMR**	**IR**	**^{13}C NMR**	**IR**
C=O	176.06	1659	176.27	1659	175.94	1658	176.11	1660
C-4	120.62	----	118.85	----	117.45	----	116.26	----
C-5	117.08	----	118.10	----	120.41	----	116.41	----
NH	----	3148	----	3138	----	3171	----	3160

The ^{13}C NMR spectra were measured in $CDCl_3$ (δ), while the IR spectra were executed in CCl_4 (cm^{-1}).

We were successful in confirming the structure of compound **134a** by the means of NOE experiments (Table 9). Nevertheless, ^{15}N NMR was the most important method to confirm the structure of heterocycle **134a**, which revealed two characteristic signals at –315 and –214 ppm (nitrogen shielding referred to nitromethane). The signal at –315 belonged to nitrogen atom of the tertiary amine, which was in agreement with the published values of other tertiary amines and is quite different if compared to the parent compound **130a**.[88] The nitrogen shielding of N-3 in the thiazole moiety appeared at –214 ppm. Due to tautomerism of compounds **134a** (compare Scheme 49), no real coupling constant [$^1J(^{15}N,^1H)$] could be observed.



134a



134b

Table 9

Irradiated hydrogen	**Compound 134a, NOE effect on (%)**			**Compound 134b, NOE effect on (%)**		
	H-4	**H-6**	**H-8**	**H-4**	**H-6**	**H-8**
H-4	----	2.0	0.6	----	1.7	0.0
H-6	7.3	----	2.6	11.8	----	5.0
H-8	0.9	1.3	----	2.8	3.7	----

However, the conformation of the piperidine group and the structure of bifunctional thiazole **134b** was determined by the X-ray crystallographic analysis, in which the piperidine group had a chair conformation (Figure 12).

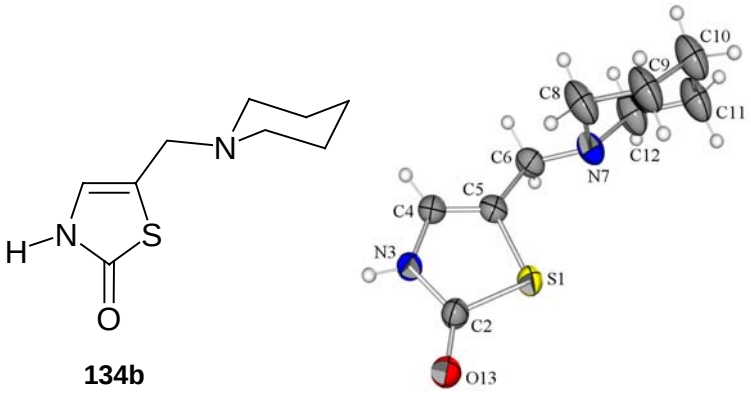


Figure 12 ORTEP drawing of compound **134b**

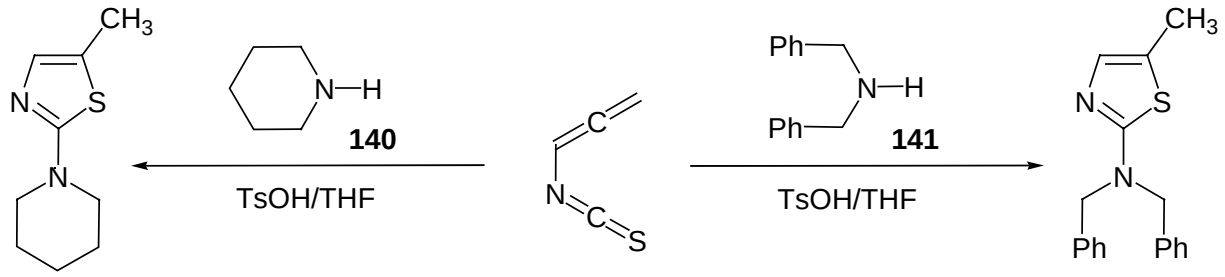
Compound **134b** could be crystallized by the diffusion-controlled method from *n*-hexane and diethyl ether at 25 °C as white plates. Crystals are monoclinic, space group *P*2(1)/*c*, with $Z = 4$.

The X-ray diffraction data of compound **134b** revealed the bond lengths of C(2)–N(3), S(1)–C(2) and C(2)–O(13) to be 134.6(3), 175.8(2), and 123.7(3) pm, respectively. Additionally, it was found that carbon C(2) has sp^2 hybridization [the sum of angles 360.0(26)°]. These data are in agreement with published results of compounds with a similar structure.[89]

Since it was difficult to get compound **130d** as a free base in an organic layer, we treated **130d** with sodium hydrogencarbonate in solution of THF and water (1:1), see Scheme 47. The free base (*N,N*-dimethyl hydroxylamine) was ceased and reacted with the excess allene **4a** to afford one major product **133d**.[90] When the same reaction was repeated using an excess amount of the free base, neither **133d**[90] nor **134d** was detected.

Although the spectroscopic data [^{1}H NMR, ^{13}C NMR, IR, GC–MS, elemental analyses (**133b**, **133c**), ESI–MS (**133b**)] proved the structures of compounds **133b** and **133c**, we found an

alternative method for their preparations by reacting piperidine **140** or dibenzylamine **141** with the ITC **4a** in the presence of toluene-4-sulfonic acid monohydrate in solution of THF and H_2O for three days at room temperature (Scheme 49).



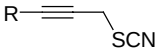
133b (43%) **4a** **133c** (82%)

Scheme 49

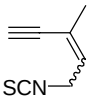
3 Summary

In this work the following goals were achieved

I. Synthesis of the New Propargyl Thiocyanates and Pent-2-en-4-ynyl Isothiocyanates (ITCs)



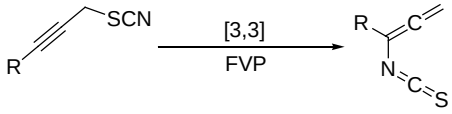
R = –SMe **24** (100%)
R = $–CH_2–O–(CH_2)_2–O–(CH_2)_2–OH$ **37** (88%)
R = $–CH=CMe_2$ **50** (92%)



***Z*,*E*-59** (84%)

II. Thermolysis Studies

The [3,3] sigmatropic rearrangement of different substituted propargyl thiocyanates, the double [3,3] sigmatropic rearrangement of enynyl ITCs, their succeeding reactions like [1,5] sigmatropic proton shift or electrocyclic ring closure were mechanistically studied by flash vacuum pyrolysis (FVP) or thermolysis in solution.



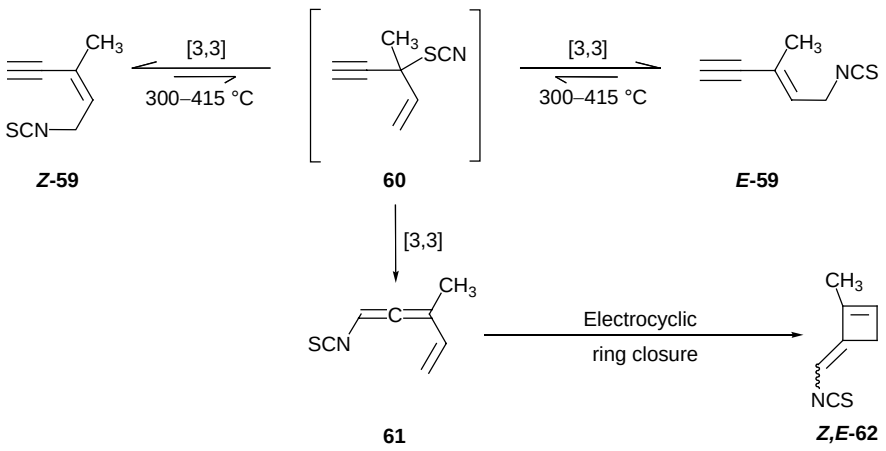
R = $–CH_2OMe$ **20** **21**
R = –SMe **24** **25**

[3,3] / FVP

FVP of compounds **20** and **24**

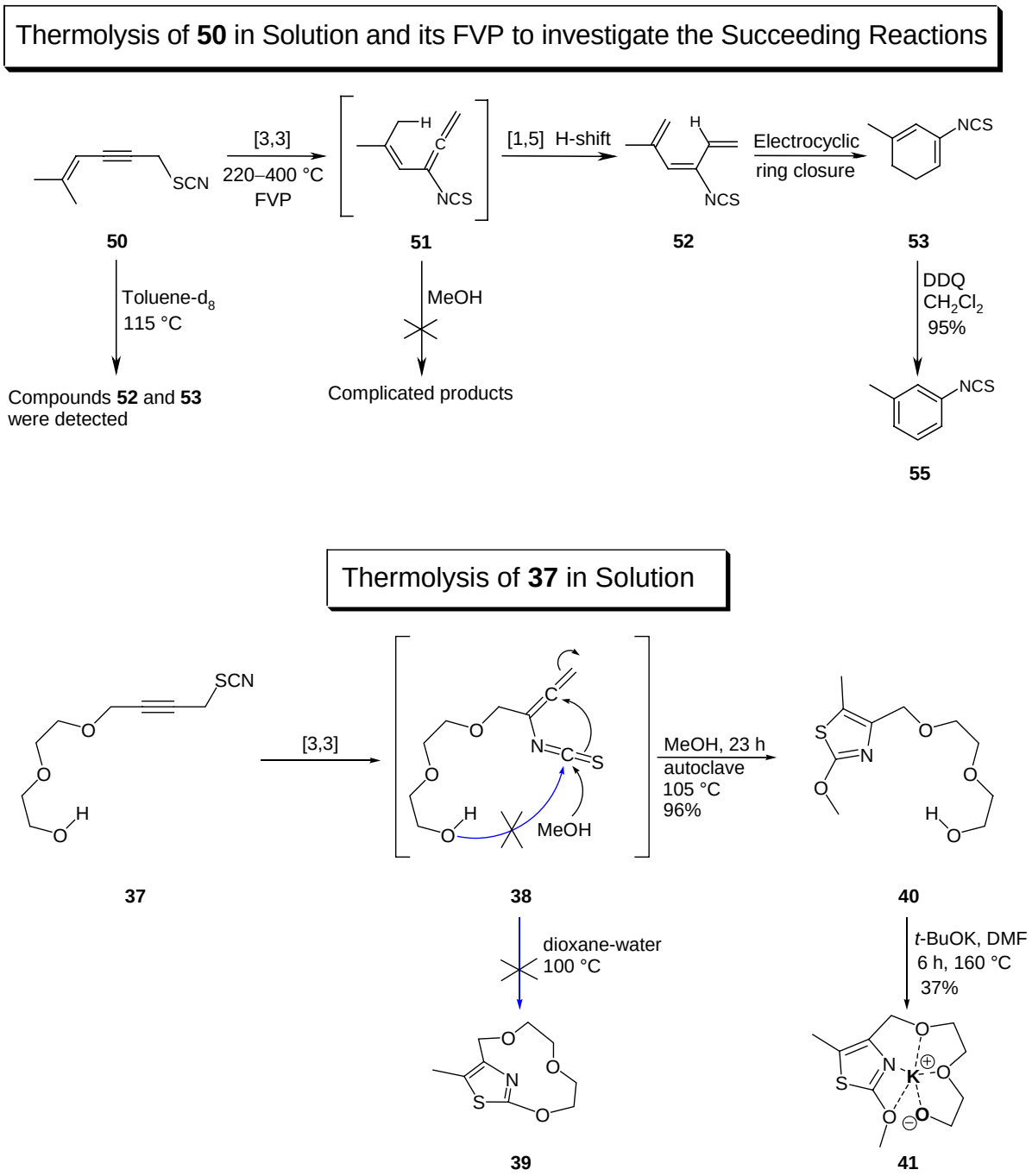
ITC **21** was separated by flash chromatography, and renewd thermolysis was done to study the thermal equilibrium between the propargyl thiocyanate **20** and ITC **21**, which was found to be **20**/**21** = 4:96.

FVP of Enynyl ITC ***Z*,*E*-59** and its Succeeding Reactions



***Z*-59** **60** ***E*-59**

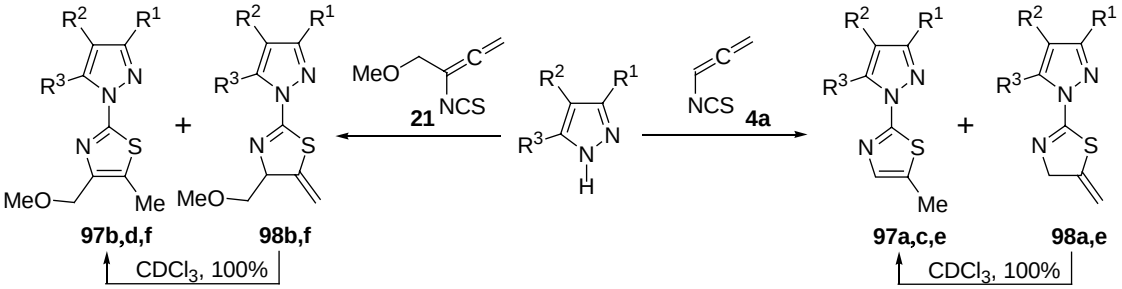
61 ***Z*,*E*-62**



III. Succeeding Reactions of Allenyl ITCs: Syntheses of New Substituted Thiazoles and Other Heterocycles

α) Pyrazoles **94a–c**, imidazoles **95a,b**, and benzimidazole **96** were treated with allenes **4a** and/or **21** furnishing substituted aromatic thiazoles **97a–i** in addition to the nonaromatic thiazoles **98a,b,e–g,i**. The latter were rearranged to the more stable aromatic compounds **98a,b,e–g,i** (in $CDCl_3$).

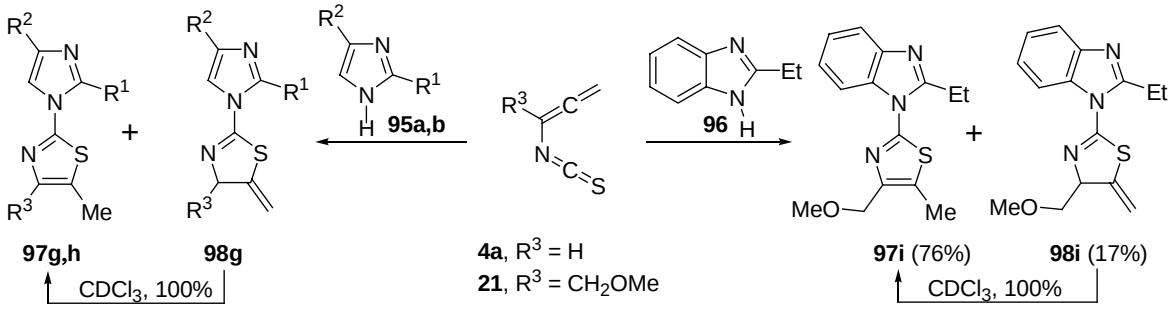
Reaction of Pyrazole Derivatives **94a–c** with ITC **4a** and **21**



97	**98**	R^1	R^2	R^3	**97**	**98**
b (39%)	**b** (46%)	Me	Me	Me	**a** (66%)	**a** (22%)
d (88%)	----	Ph	H	H	**c** (91%)	----
f (50%)	**f** (30%)	Me	H	Me	**e** (49%)	**e** (33%)

The regiochemistry of thiazole **97c** was proved by the X-ray analysis.

Reaction of Imidazole Derivatives **95a,b** and Benzimidazole **96** with ITCs **4a**/**21**

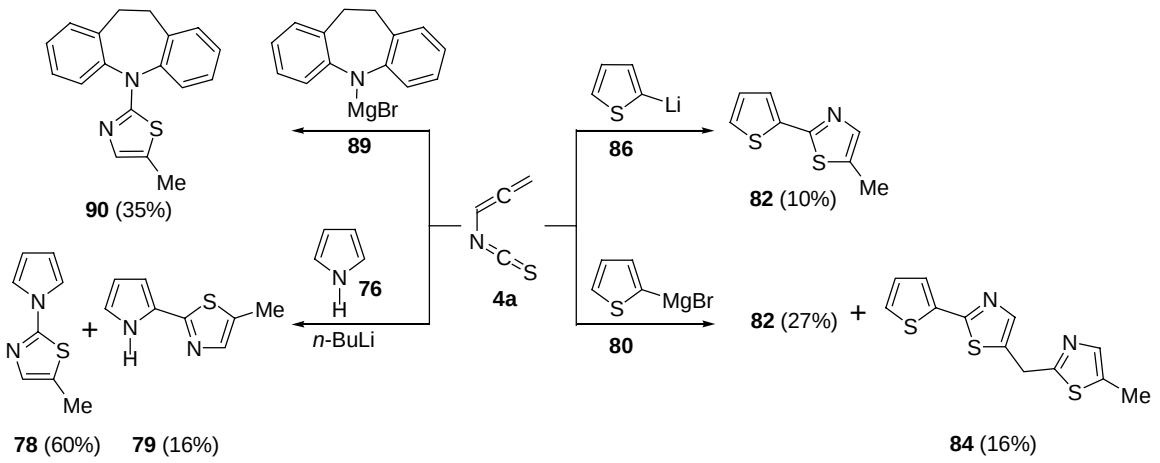


R^1	R^2	R^3	**97**	**98**
Et	Me	CH_2OMe	**g** (79%)	**g** (3%)
H	NO_2	H	**h** (68%)	**----**

The regiochemistry of thiazole **97h** was assigned by the X-ray crystallography study.

β) Treatment of pyrrole **76**, thiophene **85** or dibenzoazepine **88** with ITC **4a** recover the same starting material **76**, **85**, and **88**. The nucleophilicity of the latter compounds was increased upon their treatment with a strong base such as *n*-butyllithium or isopropylmagnesium bromide to generate anions, which yielded heterocycles **78**, **79**, **82**, **84**, and **90**.

Reaction of Pyrrole Salt, Thiophene Salts, and Dibenzoazepine Salt with ITC **4a**



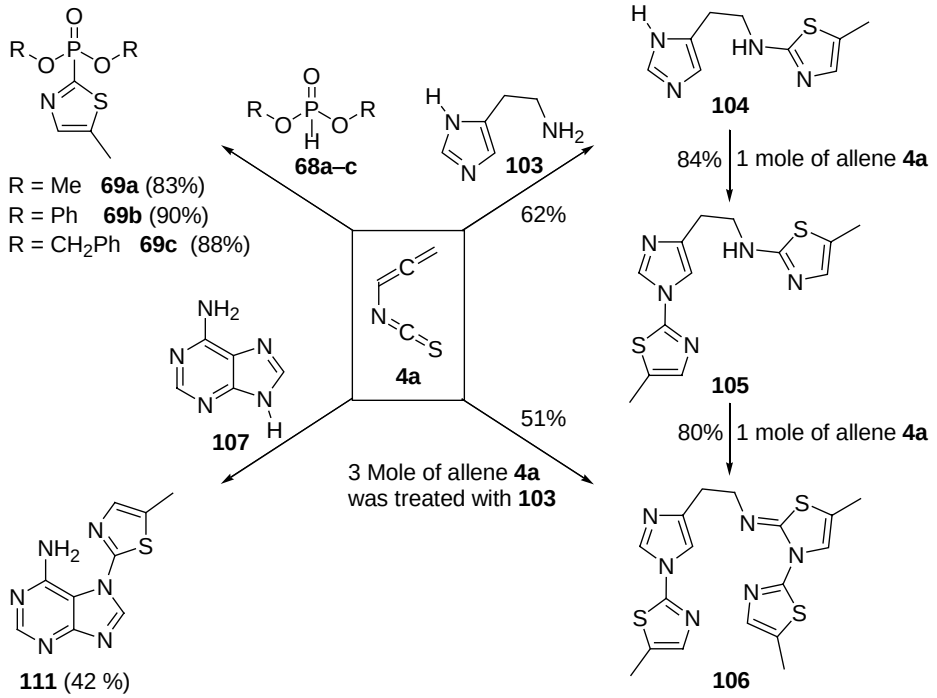
γ) Dialkyl or diphenyl phosphites **68a–c** (R = CH_3, Ph, CH_2Ph) were treated with allenyl ITC **4a** to generate the first examples of aromatic thiazoles **69a**, **69b**, and **69c** bearing a phosphorus atom of a phosphonate group at C-2 position of the thiazole ring in one pot reaction with a very good yield. Furthermore, the reactivities of the primary amino group and the imidazole ring in the histamine moiety **103** were studied by treating it with one mol of allene **4a** or two moles of allene **4a**, and finally three moles of allene **4a**. The regiochemistry and the stereochemistry of compound **106** were proved by X-ray study. Additionally, adenine **107** was also reacted with an excess amount of ITC **4a** in order to investigate the reactivity of the N-1, N-3, N-7, N-9, and the primary aromatic amine (NH_2), respectively. The regiochemistry of the obtained compound **111** was confirmed by X-ray study.

δ) A new family of thiazoles substituted at C-2 position was prepared from different nucleophiles such as hydrazoic acid. Huisgen[82] reported the reaction of hydrazoic acid with isothiocyanate derivatives to form 5-mercapto-tetrazole derivatives via the dipolar cycloaddition of 1,3-dipoles (i.e. azide) to a dipolarophile (i.e. the C=N bond of the ITC group in **4a**). Surprisingly, we did not get **116** but the unexpected and very interesting compound **115**. A proposed mechanism was suggested for this reaction.

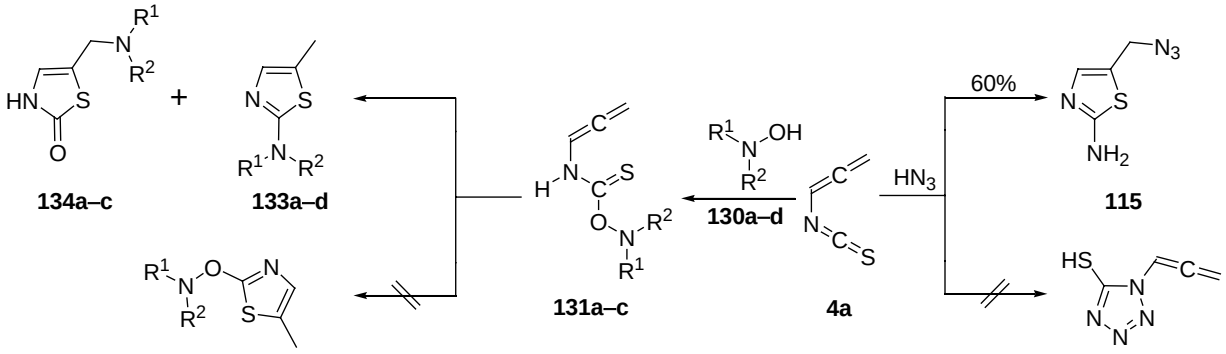
N,*N*-Disubstituted hydroxylamines **130a–d** were reacted with allene **4a** to furnish two unexpected bifunctional thiazoles **133a–d** and **134a–d** without any formation of the trivial thiazole **132**. This reaction normally undergoes via intermediates **131**, which was detected in the NMR experiment using $CDCl_3$ as a solvent.

The structure of compounds **115** and **134b** was proved by the X-ray study.

Reaction of Phosphites **68**, Histamines **103–105**, and Adenine **107** with ITC **4a**



Reaction of Hydrazoic Acid and *N*,*N*-Disubstituted Hydroxylamine **130a–d** with ITC **4a**



R^1	R^2	**131**	**133**	**134**
Et	Et	**a** (86%)	**a** (29%)	**a** (55%)
–$(CH_2)_2$–		**b** (83%)	**b** (30%)	**b** (40%)
CH_2Ph	CH_2Ph	**c** (80%)	**c** (33%)	**c** (35%)
Me	Me	----	**d** (49%)	**----**

In conclusion, it was shown that a variety of allenyl isothiocyanates are easily accessible by rearrangement reactions and highly reactive. These cumulenes lead to several succeeding products, especially to thiazoles.

4 Experimental Section

4.1 Instrumentation

Melting points were measured on BOETIUS apparatus from PENTAKON company, Dresden. Melting points were not corrected.

IR spectra were measured using FT-IR apparatus of type BRUKER IFS 28. The dissolved samples were recorded at room temperature in the wave number range from 400–4000 cm^{-1}. In some cases, only the main functional groups were reported.
Compounds ***trans/cis*-45**, **49**, **50**, **53**, ***Z/E*-59**, ***Z/E*-62**, **104**, **105**, **111**, **115**, and **133a** were recorded with a Perkin-Elmer FT-IR 1000 spectrometer as neat samples or by using a KBr disk at the Inorganic Chemistry Department, TU-Chemnitz.

NMR spectra were measured on a wide-band spectrometer-GEMINI 300 from VARIAN company. ^{1}H spectra were done on 300 MHz and ^{13}C on 75 MHz. All measurements were performed at room temperature if not otherwise mentioned. Internal standard was TMS ($\delta = 0$) or solvent signals recalculated relative to TMS. The multiplicities of ^{13}C signals were determined by the aid of gated spectra and/or DEPT 135 experiments. ^{15}N NMR spectrum was recorded without proton decoupling on spectrometer-GEMINI 2000 from VARIAN operating at 30.40 MHz. Nitromethane was employed as external reference (δ = 0 ppm) without susceptibility correction using an inner capillary tube of the standard.

Mass spectrometry ESI-MS spectra were obtained with a Mariner system 5229 spectrometer (Applied Biosystems).

GC–MS spectra were taken on a quadruple mass spectrometer (70 eV) of type GC–MS-QP 5000 from SHIMADZU company using helium as the carrier gas. Before measurement, a gas chromatogram was done on a GC–17A apparatus from SHIMADZU company.

Quantitative elemental analyses were measured on VARIO EL ELEMENTAR ANALYSENSYSTEM GmbH (Hanau).

Gas chromatography was done on a GC apparatus of type HEWLETT-PACKARD 5890/II, using flame ionization detector with 30 m quartz capillary column HP-MS 5 (coated with 5% phenylmethyl silicon). Nitrogen was the carrier gas.

Crystal structure determinations: Crystal data for the structure of **97c**, **97h**, **106**, **111**, **115**, **134b** are mentioned in appendix A-1, A-4, A-7, A-11, A-15, and A-17, respectively. Data were collected on a Bruker Smart CCD 1k diffractometer at room temperature using Mo-Kα radiation (λ = 0.71073 Å). Reflections were collected in the omega scan modus in 0.4° steps and an exposion time of 30 seconds per frame. The structure was solved by direct methods using SHELXS-97. The structure was refined by full-matrix least-squares procedures on F^2, using SHELXL-97. All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions have been refined with the atom corresponding riding model. For compound **111**, all hydrogen atom positions except at the methyl group in the methanol solvent molecule has been taken from the difference Fourier maps and refined freely. The hydrogen atom positions at C13 have been refined with a riding model. The molecule shows in the crystal a dimeric structure connected via hydrogen bridge bonding.

4.2 Working Procedures and Conditions

Flash column chromatography was performed using silica gel (0.04–0.063 mm) or neutral alumina (0.05–0.15 mm) from FLUKA company as a stationary phase. The used solvents were mentioned in the experimental section.

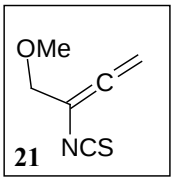
Thin layer chromatography (TLC) was carried out on POLYGRAM SIL G/UV_{254} ready foils from MACHEREY-NAGEL company.

The solvents were purified before used. Commercially available starting materials were purchased from ALDRICH, ACROS, or MERCK company.

4.3 Synthesis of Allenyl ITCs

4.3.1 FVP of 1-Methoxy-4-thiocyanato-but-2-yne 20

The FVP of 1-methoxy-4-thiocyanato-but-2-yne **20**[20] (0.10 g, 0.71 mmol) at 400 °C and 10^{-5} Torr (vaporization temperature: 70–80 °C) gave a mixture of **20** and **3-isothiocyanato-4-methoxy-buta-1,2-diene 21** (0.095 g, 0.674 mmol, 95%), with thermal equilibrium ratio of 4% and 96% of **20** and **21**, respectively.
Allenyl ITC **21** was separated by flash chromatography using *n*-hexane and diethyl ether (7:3) followed by flash vacuum pyrolysis at 400 °C and 10^{-5} Torr to reveal a mixture of **20** and **21** with the same ratio of 4:96%, respectively.



21

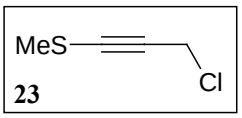
IR ($CDCl_3$): 2007 (NCS) cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 3.35 (s, 3H, OMe), 4.05 (t, ^5J = 2.1 Hz, 2H, OCH_2), 5.34 (t, ^5J = 2.2 Hz, 2H, $=CH_2$).
^{13}C NMR ($CDCl_3$): δ = 57.64 (q, OMe), 72.31 (t, OCH_2), 84.58 (t, C-1), 101.67 (s, C-3), 139.20 (s, NCS), 206.80 (s, C-2).

4.3.2 Synthesis of 1-Methylsulfanyl-3-thiocyanato-prop-1-yne 24

4.3.2.1 Preparation of 3-Chloro-1-methylsulfanyl-prop-1-yne 23

A solution of *n*-butyllithium in hexane (5.90 ml, 14.76 mmol, 2.5 M) was added dropwise to a solution of 3-chloro-prop-1-yne **22** (1.00 g, 13.42 mmol) in 13 ml of dry THF and Et_2O (6:4) at –100 °C under nitrogen. After 30 min stirring at –80 °C to –90 °C, thiocyanatomethane (1.03 g, 14.09 mmol) was added dropwise under nitrogen. After 30 min stirring at –80 °C, the reaction mixture was filtrated over a celite pad by suction, and the residue was extracted with cold diethyl ether (100 ml). The organic phase was washed with water (3×15 ml), dried ($MgSO_4$), and the solvent was removed under reduced pressure to afford **3-chloro-1-methylsulfanyl-prop-1-yne 23** (1.62 g, 13.43 mmol, 100%) as pale yellow oil. No further purification was needed for the product.

IR (CCl_4): 2931, 2200 (C≡C), 2131, 1255 cm^{-1}.



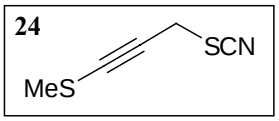
^{1}H NMR ($CDCl_3$): δ = 2.38 (s, 3H, Me), 4.26 (s, 2H, CH_2).

^{13}C NMR ($CDCl_3$): δ = 18.80 (q, Me), 31.80 (t, C-3), 79.56 (s), 87.32 (s).

4.3.2.2 Preparation of 1-Methylsulfanyl-3-thiocyanato-prop-1-yne 24

3-Chloro-1-methylsulfanyl-propyne **23** (1.00 g, 8.29 mmol) was added dropwise to a cold solution (immersed in an ice bath) of ammonium thiocyanate (1.89 g, 24.9 mmol) in DMSO (20 ml). After 15 min, the ice bath was removed, and the reaction mixture was stirred for 2.5 h. Finally, cold water (40 ml) was added followed by addition of diethyl ether (50 ml). The aqueous layer was extracted with diethyl ether (2×25 ml). The combined ethereal layers were washed with water (7×10 ml), dried ($MgSO_4$), and concentrated to give **1-methylsulfanyl-3-thiocyanato-prop-1-yne 24** (1.19 g, 8.31 mmol, 100%) as pale yellow oil. The product was clean, but it is possible to make further purification by flash chromatography from diethyl ether and *n*-hexane (2:8).

IR (CCl_4): 2931, 2197 (C≡C), 2158 (SCN), 2131, 1232 cm^{-1}.



^{1}H NMR ($CDCl_3$): δ = 2.39 (s, 3H, Me), 3.88 (s, 2H, CH_2).

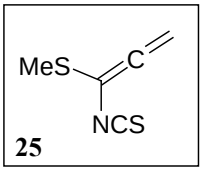
^{13}C NMR ($CDCl_3$): δ = 18.81 (q, Me), 24.60 (t, C-3), 80.41 (s), 84.09 (s), 110.92 (s, SCN).

ESI–MS ($C_5H_5NS_2$). **Calculated:** for $[M+H]^+$ 143.9880. **Found:** 143.9917.

4.3.3 FVP of 1-Methylsulfanyl-3-thiocyanato-prop-1-yne 24

FVP of 1-methylsulfanyl-3-thiocyanato-prop-1-yne **24** (0.050 g, 0.35 mmol) was executed at different temperatures (400, 350, and 300 °C) and 3×10^{-5} Torr (vaporization temperature: 80–100 °C) to give a mixture of thiocyanate **24** and **1-isothiocyanato-1-methylsulfanyl-propa-1,2-diene 25**. Composition of products was shown in Table 2. Due to the high reactivity of the allene **25**, most of it was polymerized upon purification over silica gel.

Data of allene **25**



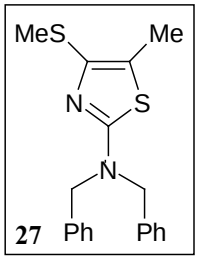
IR ($CDCl_3$): 2038 (NCS) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.34 (s, 3H, Me), 5.37 (s, 2H, $=CH_2$).

^{13}C NMR ($CDCl_3$, –50 °C): δ = 16.64 (q, Me), 85.79 (t, C-3), 100.74 (s, C-1), 137.20 (s, NCS), 205.84 (C-2).

4.3.4 Trapping of 1-Isothiocyanato-1-methylsulfanyl-propa-1,2-diene 25 with Dibenzylamine 26

By FVP of 1-methylsulfanyl-3-thiocyanato-propyne **24** (0.10 g, 0.698 mmol) at 350 °C/10^{-5} Torr, a mixture of thiocyanate **24** and allene **25** (1:4.6, see Table 2) was obtained (0.0933 g, 0.651 mmol, 93%) in 3 ml of dry THF. This mixture was added slowly at 0 °C to a solution of dibenzylamine **26** (0.33 g, 1.68 mmol) and toluene-4-sulfonic acid monohydrate (0.16 g, 0.84 mmol) in 4 ml THF and 2 ml water. After stirring 2 h at room temperature, water (10 ml) was added, and the product was extracted with diethyl ether (3×10 ml). The organic layers were combined, dried ($MgSO_4$), and concentrated by vacuum evaporation. The crude product was purified by flash chromatography using diethyl ether and *n*-hexane (2:8) to yield **2-dibenzylamino-5-methyl-4-methylsulfanyl-thiazole 27** (0.088 g, 0.26 mmol, 37%) as colorless oil.



IR ($CDCl_3$): 3088, 2924, 1523, 1210 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.29 (s, 3H, Me), 2.48 (s, 3H, Me), 4.61 (s, 4H, 2×CH_2), 7.25–7.39 (m, 10H, 2×Ph).

^{13}C NMR ($CDCl_3$): δ = 11.89 (q, Me), 17.18 (q, Me), 53.10 (t, 2×CH_2), 117.09 (s), 127.45 (d, 2×Ph_p), 127.83 (d, 4×Ph), 128.55 (d, 4×Ph), 136.81 (s, 2×Ph_i), 139.92 (s), 167.37 (s, C-2).

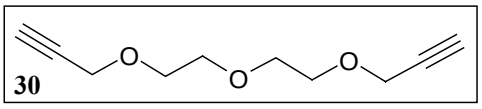
ESI–MS ($C_{19}H_{20}N_2S_2$). **Calculated:** for $[M+H]^+$ 341.1092. **Found:** 341.1070

4.3.5 Synthesis of 2-[2-(4-Thiocyanato-but-2-ynyloxy)-ethoxy]-ethanol 37

4.3.5.1 Preparation of 3-[2-(2-Prop-2-ynyloxy-ethoxy)-ethoxy]-propyne 30 and 2-(2-Prop-2-ynyloxy-ethoxy)-ethanol 31

Sodium hydroxide (3.70 g, 92.43 mmol) was added to a mixture of 3-bromo-propyne **28** (10.00 g, 84.03 mmol) and 2-(2-hydroxy-ethoxy)-ethanol **29** (9.80 g, 92.43 mmol) at –15 °C. After stirring for 2 h at 10–20 °C, diethyl ether (200 ml) was added followed by addition of water (25 ml). The organic layer was separated, washed with water (3×25 ml), dried ($MgSO_4$), and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography using diethyl ether to generate firstly **3-[2-(2-prop-2-ynyloxy-ethoxy)-ethoxy]-propyne 30**[23] (2.29 g, 12.57 mmol, 15%) as colorless oil and then **2-(2-prop-2-ynyloxy-ethoxy)-ethanol 31**[24] (6.29 g, 43.70 mmol, 52%) as colorless oil.

Data of **30**[23]



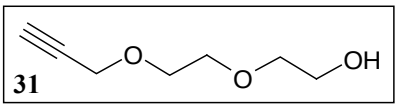
30

IR (CCl_4): 3312 (≡C–H), 2952, 2848, 2118 (C≡C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.39 (t, ^4J = 2.4 Hz, 2H, 2×C≡CH), 3.62 (m, 8H, 4×CH_2), 4.13 (d, ^4J = 2.4 Hz, 4H, 2×–OCH_2C≡CH).

^{13}C NMR ($CDCl_3$): δ = 58.15 (t, C), 68.85 (t, C), 70.19 (t, C), 74.40 (s, C), 79.44 (d, C).

Data of **31**[24]



31

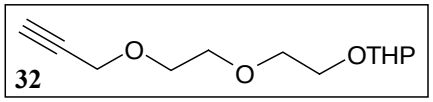
IR (CCl_4): 3607 (OH), 3312 (≡C–H), 2954, 2867, 2119 (C≡C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.41 (t, ^4J = 2.4 Hz, 1H, C≡C–H), 3.02 (br, 1H, OH), 3.52 (t, J = 3.9 Hz, 2H, CH_2), 3.62 (m, 4H, 2×CH_2), 3.65 (t, J = 4.2 Hz, 2H, CH_2), 4.13 (d, ^4J = 2.4 Hz, 2H, –OCH_2C≡CH).

^{13}C NMR ($CDCl_3$): δ = 58.17 (t), 61.38 (t), 68.89 (t), 69.93 (t), 72.38 (t), 74.63 (s), 79.27 (d).

4.3.5.2 Preparation of 2-[2-(2-Prop-2-ynyloxy-ethoxy)-ethoxy]-tetrahydro-pyran 32

2-(2-Prop-2-ynyloxy-ethoxy)-ethanol **31**[24] (2.0 g, 13.89 mmol) was mixed with 3,4-dihydro-2*H*-pyran (1.28 g, 15.28 mmol) and then cooled in ice bath for 10 minutes. Concentrated HCl (0.01 ml) was added and the reaction mixture was stirred overnight. Diethyl ether (100 ml) was added and the organic part was washed with water (3×25 ml), dried ($MgSO_4$), and concentrated under vacuum. The crude product was purified by flash chromatography using diethyl ether and *n*-hexane (1:1) to furnish **2-[2-(2-prop-2-ynyloxy-ethoxy)-ethoxy]-tetrahydro-pyran 32** as colorless oil (2.79 g, 12.24 mmol, 88%).

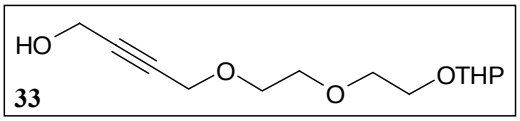


32

IR ($CDCl_3$): 3307 (≡C–H), 2966, 2851, 2121 (C≡C) cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 1.46–1.80 (m, 6H, 3×CH_2), 2.39 (t, ^4J = 2.4 Hz, 1H, C≡C–H), 3.41–3.63 (m, 4H, 2×CH_2), 3.65 (s, 4H, 2×CH_2), 3.78–3.85 (m, 2H, –OCH_2 [THP]), 4.16 (d, ^4J = 2.4 Hz, 2H, –OCH_2C≡CH), 4.58 (dd, ^3J = 4.1 Hz, ^3J = 2.9 Hz, 1H, –OCHO–).
^{13}C NMR ($CDCl_3$): δ = 19.33 (t), 25.29 (t), 30.42 (t), 58.25 (t), 62.04 (t), 66.49 (t), 68.98 (t), 70.29 (t), 70.42 (t), 74.42 (s), 79.54 (d), 98.78 (d).

4.3.5.3 Preparation of 4-{2-[2-(2-Tetrahydro-pyran-2-yloxy)-ethoxy]-ethoxy}-but-2-yn-1-ol 33

A solution of *n*-butyllithium (4.82 ml, 12.06 mmol, 2.5 M) was added slowly to a stirred solution of 2-[2-(2-prop-2-ynyloxy-ethoxy)-ethoxy]-tetrahydro-pyran **32** (2.50 g, 10.96 mmol) in 20 ml of dry THF at –90 °C. Paraformaldehyde (1.31 g, 43.86 mmol) was added at 0 °C. After 2 h, the reaction mixture was heated for 90 min at 35–40 °C. The mixture was allowed to cool down to room temperature, then a saturated solution of ammonium chloride (25 ml) and thereafter diethyl ether (100 ml) was added. The organic layer was separated, and the aqueous layer was extracted again with diethyl ether (2×50 ml). The organic extracts were collected, dried ($MgSO_4$), and the solvent was removed under vacuum. The product was purified by flash chromatography using diethyl ether to provide **4-{2-[2-(2-tetrahydro-pyran-2-yloxy)-ethoxy]-ethoxy}-but-2-yn-1-ol 33** (1.73 g, 6.71 mmol, 61%) as colorless oil.



33

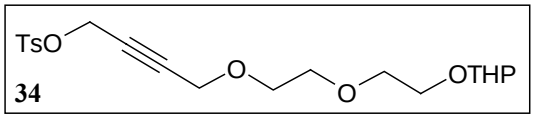
IR ($CDCl_3$): 3611 (OH), 2967, 2873 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.46–1.87 (m, 6H, 3×CH_2), 1.94 (br, 1H, OH), 3.46–3.54 (m, 1H), 3.59–3.73 (m, 7H), 3.83–3.91 (m, 2H, –OCH_2 [THP]), 4.24 (t, ^5J = 1.8 Hz, 2H), 4.30 (t, ^5J = 1.5 Hz, 2H), 4.65 (dd, ^3J = 4.2 Hz, ^3J = 2.7 Hz, 1H, –OCHO–).

^{13}C NMR ($CDCl_3$): δ = 19.19 (t), 25.15 (t), 30.27 (t), 50.42 (t), 58.43 (t), 62.02 (t), 66.41 (t), 68.83 (t), 70.18 (t), 70.28 (t), 80.84 (s), 84.96 (s), 98.72 (d).

4.3.5.4 Preparation of Toluene-4-sulfonic Acid 4-{2-[2-(2-Tetrahydro-pyran-2-yloxy)-ethoxy]-ethoxy}-but-2-ynyl Ester 34

Potassium hydroxide (0.651 g, 11.64 mmol) was added to a stirred solution of *p*-toluenesulfonyl chloride (0.89 g, 4.65 mmol) and 4-{2-[2-(2-tetrahydro-pyran-2-yloxy)-ethoxy]-ethoxy}-but-2-yn-1-ol **33** (1.0 g, 3.88 mmol) in 30 ml of diethyl ether at 0 °C. The reaction mixture was stirred for 90 min at this temperature. Water (30 ml) was added and the separated organic layer was washed with water (2×30 ml), dried ($MgSO_4$) and evaporated to obtain **toluene-4-sulfonic acid 4-{2-[2-(2-tetrahydro-pyran-2-yloxy)-ethoxy]-ethoxy}-but-2-ynyl ester 34** as colorless oil (1.57 g, 3.81 mmol, 98%)



34

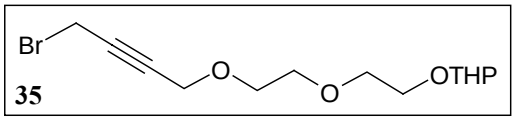
IR (CCl_4): 2945, 2871, 1599, 1380 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.49–1.82 (m, 6H, 3×CH_2), 2.43 (s, 3H, Me), 3.43–3.51 (m, 2H, CH_2), 3.55 (dt, *J* = 5.6 Hz, *J* = 2.8 Hz, 2H, CH_2), 3.62 (t, *J* = 4.8 Hz, 2H, CH_2), 3.66 (t, *J* = 5.0 Hz, 2H, CH_2), 3.80–3.87 (m, 2H, –OCH_2 [THP]), 4.08 (t, ^5J = 1.8 Hz, 2H, –$OCH_2C{\equiv}C$–), 4.59 (dd, ^3J = 4.2 Hz, ^3J = 2.7 Hz, 1H, –OCHO–), 4.71 (t, ^5J = 1.8 Hz, 2H, $TsOCH_2$), 7.33 (d, *J* = 8.7 Hz, 2H, 2×Ar-H), 7.78 (d, *J* = 8.4 Hz, 2H, 2×Ar-H).

^{13}C NMR ($CDCl_3$): δ = 19.25 (t), 21.46 (q, Me), 25.14 (t), 30.29 (t), 57.69 (t), 58.07 (t), 62.00 (t), 66.35 (t), 68.95 (t), 70.07 (t), 70.29 (t), 77.85 (s), 85.24 (s), 98.68 (d), 127.86 (d, 2×Ph), 129.63 (d, 2×Ph), 132.63 (s), 144.94 (s).

4.3.5.5 Preparation of 2-{2-[2-(4-Bromo-but-2-ynyloxy)-ethoxy]-ethoxy}-tetrahydro-pyran 35

Toluene-4-sulfonic acid 4-{2-[2-(2-tetrahydro-pyran-2-yloxy)-ethoxy]-ethoxy}-but-2-ynyl ester **34** (0.65 g, 1.58 mmol) was added to a stirred solution of anhydrous lithium bromide (0.55 g, 6.32 mmol) in 20 ml of dry DMSO. After 1 h at room temperature, cold water (20 ml) was added followed by addition of diethyl ether (50 ml). The organic layer was separated, and the aqueous phase was extracted with diethyl ether (2×25 ml). The combined organic layers were washed with water (7×25 ml), dried ($MgSO_4$), and concentrated to give **2-{2-[2-(4-bromo-but-2-ynyloxy)-ethoxy]-ethoxy}-tetrahydro-pyran 35** as colorless oil (0.43 g, 1.34 mmol, 84%). Further purification can be done by flash chromatography using diethyl ether.



35

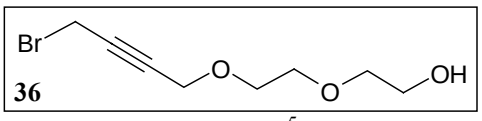
IR (CCl_4): 2945, 2871, 1349 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.45–1.81 (m, 6H, 3×CH_2), 3.40–3.47 (m, 1H), 3.51–3.62 (m, 1H), 3.62 (s, 6H, 3×CH_2), 3.77–3.83 (m, 2H, –OCH_2 [THP]), 3.89 (t, ^5J = 1.8 Hz, 2H, $BrCH_2$), 4.20 (t, ^5J = 1.8 Hz, 2H, –$OCH_2C{\equiv}C$–), 4.56 (dd, ^3J = 4.4 Hz, ^3J = 2.9 Hz, 1H, –OCHO–).

^{13}C NMR ($CDCl_3$): δ = 14.10 (t), 19.32 (t), 25.27 (t), 30.41 (t), 58.51 (t), 62.03 (t), 66.46 (t), 69.11 (t), 70.26 (t), 70.41 (t), 81.22 (s), 82.75 (s), 98.76 (d).

4.3.5.6 Preparation of 2-[2-(4-Bromo-but-2-ynyloxy)-ethoxy]-ethanol 36

2-{2-[2-(4-Bromo-but-2-ynyloxy)-ethoxy]-ethoxy}-tetrahydro-pyran **35** (0.36 g, 1.12 mmol) was mixed with methanol (4 ml). Concentrated H_2SO_4 (0.18 ml) was added dropwise over few minutes. After 1 h stirring at room temperature, diethyl ether (40 ml) was added to the reaction mixture followed by addition of saturated solution of sodium carbonate (10 ml). The organic layer was separated, and the aqueous phase was extracted with chloroform (2×10 ml). The combined organic layers were washed with saturated solution of sodium carbonate (2×10 ml), dried ($MgSO_4$), and the solvent was removed under vacuum to afford **2-[2-(4-bromo-but-2-ynyloxy)-ethoxy]-ethanol 36** (0.26 g, 1.11 mmol, 99%) as colorless oil. Further purification can be carried out by flash chromatography using diethyl ether.



36

IR (CCl_4): 3608 (OH), 2948, 2870, 1349 cm^{-1}.

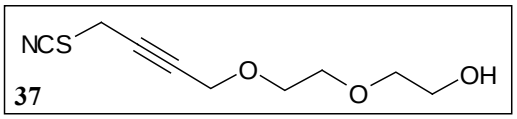
^{1}H NMR ($CDCl_3$): δ = 2.03 (br, 1H, OH), 3.61 (t, *J* = 4.4 Hz, 2H, CH_2), 3.69 (s, 4H, 2×CH_2), 3.74 (t, *J* = 4.5 Hz, 2H, CH_2), 3.94 (t, ^5J = 2 Hz, 2H, $BrCH_2$), 4.26 (t, ^5J = 2 Hz, 2H, –$OCH_2C{\equiv}C$–).

^{13}C NMR ($CDCl_3$): δ = 14.10 (t), 58.49 (t), 61.45 (t), 69.06 (t), 69.97 (t), 72.39 (t), 81.45 (s), 82.46 (s).

ESI–MS ($C_8H_{13}O_3Br$). $[M+H]^+$ 236.98 (^{79}Br), $[M+H]^+$ 238.98 (^{81}Br)

4.3.5.7 Preparation of 2-[2-(4-Thiocyanato-but-2-ynyloxy)-ethoxy]-ethanol 37

2-[2-(4-Bromo-but-2-ynyloxy)-ethoxy]-ethanol **36** (0.25 g, 1.06 mmol) was added dropwise to a stirred solution of ammonium thiocyanate (0.24 g, 3.17 mmol) in methanol (10 ml). After 18 h at room temperature, the solvent was removed under vacuum, and CH_2Cl_2 (10 ml) was added to the residue. The suspension was filtrated over a celite pad and extracted with CH_2Cl_2 (3×10 ml). The organic solutions were collected, and the solvent was removed under vacuum to furnish **2-[2-(4-thiocyanato-but-2-ynyloxy)-ethoxy]-ethanol 37** (0.22 g, 1.02 mmol, 96%) as pale purple oil. Further purification can be executed by flash chromatography using diethyl ether and THF (1:1).



37

IR ($CDCl_3$): 3590 (OH), 2929, 2872, 2160 (SCN) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.40 (s, 1H, OH), 3.60 (t, *J* = 4.5 Hz, 2H, CH_2), 3.67–3.73 (m, 4H, 2×CH_2), 3.74 (t, *J* = 4.5 Hz, 2H, CH_2), 3.79 (t, ^5J = 1.95 Hz, 2H, $NCSCH_2$), 4.27 (t, ^5J = 1.95 Hz, 2H, –$OCH_2C{\equiv}C$–).

^{13}C NMR ($CDCl_3$): δ = 23.09 (t), 58.51 (t), 61.66 (t), 69.26 (t), 70.13 (t), 72.40 (t), 78.43 (s) 83.26 (s), 110.82 (s, SCN).

ESI–MS ($C_9H_{13}NO_3S$). **Calculated:** for $[M+H]^+$ 216.0640. **Found:** 216.0624.

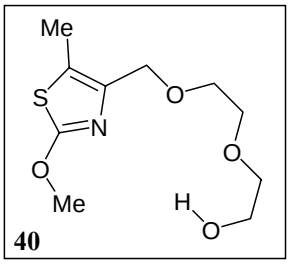
4.3.6 Trapping of 2-[2-(2-Isothiocyanato-buta-2,3-dienyloxy)-ethoxy]-ethanol 38 with Methanol

- Method **A**

2-[2-(4-Thiocyanato-but-2-ynyloxy)-ethoxy]-ethanol **37** (0.13 g, 0.60 mmol) was dissolved in a mixture of DMSO and methanol (40 ml, 1:1/volume ratio). The reaction mixture was stirred at 130 °C for 96 h. The solvents were removed under reduced pressure and the crude product was purified by flash column chromatography using THF and diethyl ether (4:6) to yield **2-[2-(2-methoxy-5-methyl-thiazol-4-ylmethoxy)-ethoxy]-ethanol 40** (0.049 g, 0.198 mmol, 33%) as pale yellow oil.

- Method **B**

2-[2-(4-Thiocyanato-but-2-ynyloxy)-ethoxy]-ethanol **37** (0.15 g, 0.70 mmol) was dissolved in methanol (150 ml) and heated at 105 °C in an autoclave for 23 h. The methanol was removed under vacuum and the crude product was purified by flash chromatography using THF and diethyl ether (4:6) to afford **2-[2-(2-methoxy-5-methyl-thiazol-4-ylmethoxy)-ethoxy]-ethanol 40** (0.17 g, 0.67 mmol, 96%) as pale yellow oil.



40

IR ($CDCl_3$): 3244 (OH), 2933, 2868, 1534, 1116 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.29 (s, 3H, Me), 2.83 (br, 1H, OH), 3.58 (t, *J* = 4.5 Hz, 2H, CH_2), 3.66 (t, *J* = 2.9 Hz, 2H, CH_2), 3.67 (t, *J* = 2.9 Hz, 2H, CH_2), 3.71 (t, *J* = 4.4 Hz, 2H, CH_2), 3.99 (s, 3H, OMe), 4.41 (s, 2H, thiazole–CH_2O–).

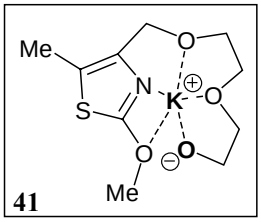
^{13}C NMR ($CDCl_3$): δ = 11.11 (q, Me), 57.93 (q, OMe), 61.64 (t), 65.93 (t), 69.30 (t), 70.36 (t), 72.46 (t), 123.49 (s), 141.60 (s), 171.59 (s, C-2).

ESI–MS ($C_{10}H_{17}NO_4S$). **Calculated:** for $[M+H]^+$ 248.0951. **Found:** 248.0927.

Anal. Calcd for $C_{10}H_{17}NO_4S$ (247.32): C, 48.57; H, 6.93; N, 5.66; S, 12.96. **Found:** C, 48.01; H, 6.64; N, 5.60; S, 12.02.

4.3.7 Preparation of Potassium 2-[2-(2-Methoxy-5-methyl-thiazol-4-ylmethoxy)-ethoxy]-ethanolate 41

2-[2-(2-Methoxy-5-methyl-thiazol-4-ylmethoxy)-ethoxy]-ethanol **40** (0.10 g, 0.40 mmol) was added to a stirred solution of potassium 2-methyl-propan-2-olate (0.050 g, 0.44 mmol) in 15 ml dry DMF at room temperature. After 6 h at 160 °C, DMF was removed under reduced pressure (10^{-3} Torr) and the residue was extracted with dry CH_2Cl_2 (3×10 ml). Dichloromethane was removed under vacuum to give **potassium 2-[2-(2-methoxy-5-methyl-thiazol-4-ylmethoxy)-ethoxy]-ethanolate 41** (0.069 g, 0.24 mmol, 60%) as brown oil. The crude product was purified by simple washing with dry diethyl ether (3×20 ml) to give the remaining compound **41** (0.043 g, 0.15 mmol, 37%) after removal of the ether as pale yellow oil.



41

IR ($CDCl_3$): 2929, 2867, 1655, 1048 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.17 (s, 3H, Me), 3.31 (s, 3H, OMe), 3.56 (t, *J* = 2.9 Hz, 2H, CH_2), 3.58 (t, *J* = 2.9 Hz, 2H, CH_2), 3.64 (t, *J* = 4.5 Hz, 2H, CH_2), 3.72 (t, *J* = 4.5 Hz, 2H, CH_2), 4.32 (s, 2H, thiazole–CH_2O–).

^{13}C NMR ($CDCl_3$): δ = 12.08 (q, Me), 29.72 (q, OMe), 61.63 (t), 62.01 (t), 69.75 (t), 70.23 (t), 72.45 (t), 113.45 (s), 127.21 (s), 171.07 (s, C-2).

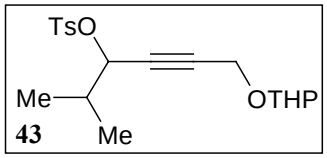
ESI–MS ($C_{10}H_{16}KNO_4S$). **Calculated:** for $[M+H]^+$ 286.0510. **Found:** 286.0573.

4.3.8 Synthesis of 2-Methyl-6-thiocyanato-hex-2-en-4-yne 50

4.3.8.1 Preparation of Toluene-4-sulfonic Acid 1-Isopropyl-4-(tetrahydro-pyran-2-yloxy)-but-2-ynyl Ester 43

Potassium hydroxide (6.60 g, 118 mmol) was added to a stirred solution of tosyl chloride (6.29 g, 33.0 mmol) and 2-methyl-6-(tetrahydro-pyran-2-yloxy)-hex-4-yn-3-ol[33] **42** (5.00 g, 23.6 mmol) in 30 ml of diethyl ether at 0 °C. The reaction mixture was stirred for 90 min at this temperature followed by stirring overnight under nitrogen. Water (30 ml) was added and the separated organic layer was washed with water (2×30 ml), dried ($MgSO_4$), and evaporated to generate **toluene-4-sulfonic acid 1-isopropyl-4-(tetrahydro-pyran-2-yloxy)-but-2-ynyl**

ester 43 as pale yellow oil (8.12 g, 22.17 mmol, 94%) (Purification by distillation at 115–120 °C and 10^{-2} Torr).



43

IR ($CDCl_3$): 2945, 1599, 1391, 1189, 1026, 835 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.92 (d, ^3J = 6.9 Hz, 3H, Me), 0.97 (d, ^3J = 6.6 Hz, 3H, Me), 1.46–1.76 (m, 6H, 3×CH_2), 2.02 (m, 1H, CH), 2.40 (s, 3H, Me), 3.42–3.76 (m, 2H, –OCH_2), 4.06 (m, 2H, –$OCH_2C{\equiv}C$–), 4.62 (m, 1H, TsOCH), 4.94 (m, 1H, –OCHO–), 7.28 (d, J = 8.4 Hz, 2H, 2×Ar-H), 7.76 (d, J = 8.1 Hz, 2H, 2×Ar-H).

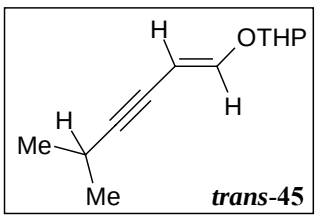
^{13}C NMR ($CDCl_3$): δ = 17.20 (q, Me), 17.30 (q, Me), 18.30 (t), 21.50 (q, Me), 25.16 (t), 30.03 (t), 33.31 (d), 53.46 (t), 61.78 (t), 76.50 (d) 79.75 (s), 84.89 (s), 96.36 (d), 127.92 (d), 129.43 (d), 134.00 (s), 144.50 (s).

Anal. Calcd for $C_{19}H_{26}O_5S$ (366.48): C, 62.27; H, 7.15; S, 8.75. **Found:** C, 61.65; H, 7.24; S, 9.23.

4.3.8.2 Preparation of *trans*- and *cis*-2-(5-Methyl-hex-1-en-3-ynyloxy)-tetrahydro-pyran 45

A solution of toluene-4-sulfonic acid 1-isopropyl-4-(tetrahydro-pyran-2-yloxy)-but-2-ynyl ester **43** (1.00 g, 2.73 mmol) and KOH (0.76 g, 13.7 mmol) in 10 ml of pyridine was refluxed under nitrogen gas for 45 minutes. After the reaction mixture was cooled to room temperature, water (30 ml) was added, and the products were extracted with diethyl ether (3×20 ml). The combined organic layers were washed with water (3×10 ml), dried ($MgSO_4$), and concentrated to give two isomers ***trans***- and ***cis*-45** in ~1:1 ratio. Flash chromatography using *n*-hexane and diethyl ether (9:1) afforded ***trans*-2-(5-methyl-hex-1-en-3-ynyloxy)-tetrahydro-pyran *trans*-45** as pale yellow oil (0.10 g, 0.51 mmol, 19%) and then ***cis*-2-(5-methyl-hex-1-en-3-ynyloxy)-tetrahydro-pyran *cis*-45** as pale yellow oil (0.11 g, 0.56 mmol, 20%).

Data of ***trans*-45**



***trans*-45**

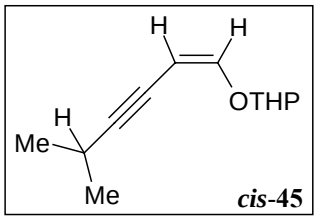
IR (neat): 2963, 1942, 1642, 960 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.14 (d, ^3J = 6.9 Hz, 6H, 2×Me), 1.51–1.86 (m, 6H, 3×CH_2), 2.63 (sept.d, ^3J = 6.9 Hz, ^5J = 2.1 Hz, 1H, H-5'),

3.52–3.82 (m, 2H, –OCH_2), 4.97 (t, ^3J = 2.7 Hz, 1H, –OCHO), 5.12 (dd, ^3J = 12.6 Hz, ^5J = 2.1 Hz, 1H, H-2'), 6.78 (dd, ^3J = 12.6 Hz, ^6J = 0.6 Hz, 1H, H-1').
^{13}C NMR ($CDCl_3$): δ = 18.19 (t), 21.15 (d, C-5'), 23.14 (q, 2×Me), 24.94 (t), 29.35 (t), 61.72 (t, C-6), 75.06 (s) 89.46 (d, C-2'), 94.44 (s), 98.26 (d, C-2), 153.47 (d, C-1').

Data of ***cis*-45**

IR (neat): 2967, 1942, 1635, 799 cm^{-1}.



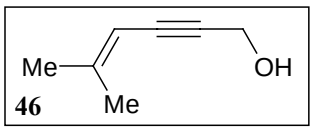
***cis*-45**

^{1}H NMR ($CDCl_3$): δ = 1.19 (d, ^3J = 6.9 Hz, 6H, 2×Me), 1.53–1.96 (m, 6H, 3×CH_2), 2.72 (sept.d, ^3J = 6.9 Hz, ^5J = 1.8 Hz, 1H, H-5'), 3.55–3.93 (m, 2H, –OCH_2), 4.63 (dd, ^3J = 6.3 Hz, ^5J = 2.1 Hz, 1H, H-2'), 5.04 (t, ^3J = 3.0 Hz, 1H, –OCHO), 6.47 (dd, ^3J = 6.3 Hz, ^6J = 0.6 Hz, 1H, H-1').
^{13}C NMR ($CDCl_3$): δ = 18.15 (t), 21.36 (d, C-5'), 23.14 (q, 2×Me), 25.07 (t), 29.34 (t), 61.66 (t, C-6), 73.50 (s) 88.04 (d, C-2'), 98.63 (d, C-2), 99.24 (s), 150.95 (d, C-1').

4.3.8.3 Preparation of 5-Methyl-hex-4-en-2-yn-1-ol 46

A solution of toluene-4-sulfonic acid 1-isopropyl-4-(tetrahydro-pyran-2-yloxy)-but-2-ynyl ester **43** (5.0 g, 13.6 mmol), anhydrous lithium bromide (0.59 g, 6.82 mmol), and lithium carbonate (1.92 g, 25.9 mmol) in 150 ml of dry DMF was refluxed for 3 h. After cooling to room temperature, the solvent was removed under vacuum and the brown crude product was purified by flash chromatography with diethyl ether and *n*-hexane (1:1) to give **5-methyl-hex-4-en-2-yn-1-ol 46**[34] as yellow oil (1.32 g, 11.98 mmol, 88%).

IR (CCl_4): 3621 (OH), 2936, 2871, 2205, 1024 cm^{-1}.

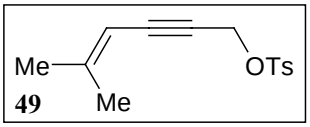


46

^{1}H NMR ($CDCl_3$): δ = 1.76 (m, 3H, Me), 1.84 (m, 3H, Me), 2.62 (br, 1H, OH), 4.35 (d, ^5J = 2.1 Hz, 2H, CH_2), 5.12 (m, 1H, =CH).
^{13}C NMR ($CDCl_3$): δ = 20.83 (q, Me), 24.64 (q, Me), 51.36 (t, C-1), 83.36 (s), 89.20 (s), 104.45 (d, C-4), 149.08 (s, C-5).

4.3.8.4 Preparation of Toluene-4-sulfonic Acid 5-Methyl-hex-4-en-2-ynyl Ester 49

Potassium hydroxide (1.53 g, 27.2 mmol) was added to a stirred solution of *p*-toluenesulfonyl chloride (2.08 g, 10.9 mmol) and 5-methyl-hex-4-en-2-yn-1-ol **46** (1.0 g, 9.08 mmol) in 50 ml of diethyl ether at 0 °C. The reaction mixture was stirred for 2 h at this temperature. Water (40 ml) was added and the separated organic layer was washed with water (3×30 ml), collected, dried ($MgSO_4$), and evaporated to yield **toluene-4-sulfonic acid 5-methyl-hex-4-en-2-ynyl ester 49** as yellow oil (2.11 g, 7.98 mmol, 88%)



49

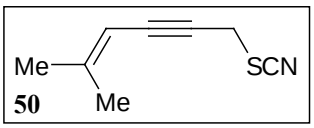
IR (neat): 2219, 1366, 1176 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.76 (m, 6H, 2×Me), 2.43 (m, 3H, Me), 4.85 (d, ^5J = 2.1 Hz, 2H, CH_2), 5.12 (m, 1H, =CH), 7.31 (d, J = 8.4 Hz, 2H, 2×Ar-H), 7.79 (d, J = 8.7 Hz, 2H, 2×Ar-H).

^{13}C NMR ($CDCl_3$): δ = 21.01 (q, Me), 21.59 (q, Me), 24.80 (q, Me), 59.01 (t, C-1'), 82.27 (s), 87.20 (s), 103.79 (d, C-4'), 128.03 (d), 129.71 (d), 133.22 (s), 144.87 (s), 151.52 (s).

4.3.8.5 Preparation of 2-Methyl-6-thiocyanato-hex-2-en-4-yne 50

To a solution of ammonium thiocyanate (0.17 g, 2.27 mmol) in DMSO (20 ml), toluene-4-sulfonic acid 5-methyl-hex-4-en-2-ynyl ester **49** (0.20 g, 0.76 mmol) in DMSO (3 ml) was added dropwise at 0 °C. After stirring at room temperature for 1 hr, 10 ml of cold water was added, and the product was extracted with 25 ml of diethyl ether. The organic layer was washed with water (7×10 ml), dried ($MgSO_4$), and concentrated to afford **2-methyl-6-thiocyanato-hex-2-en-4-yne 50** as yellow oil (0.106 g, 0.70 mmol, 96%). Purification was carried out by flash chromatography with *n*-hexane and diethyl ether (9:1).



50

IR (neat): 2159 (SCN), 1444, 1239, 817 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.81 (m, 3H, Me), 1.90 (m, 3H, Me), 3.93 (d, ^5J = 2.1 Hz, 2H, CH_2), 5.27 (m, 1H, =CH).

^{13}C NMR ($CDCl_3$): δ = 21.16 (q, Me), 24.50 (q, Me), 24.88 (t, C-6), 82.46 (s), 85.58 (s), 103.88 (d, C-3), 111.23 (s, SCN), 151.68 (s, C-2).

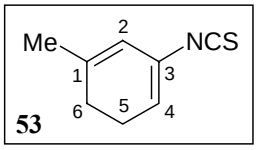
GC–MS; *m*/*z* (%): 151 [M^+] (5), 93 (57), 91 (55), 77 (100), 39 (62), (retention time: 15.82 min).

Anal. Calcd for C_8H_9NS (151.23): C, 63.53; H, 5.99; N, 9.26; S, 21.20. **Found:** C, 63.59; H, 6.04; N, 9.32; S, 21.25.

4.3.9 FVP of 2-Methyl-6-thiocyanato-hex-2-en-4-yne 50

FVP of **50** (0.10 g, 0.66 mmol) was carried out at different temperatures (400, 350, 300, 270 and 220 °C) and 10^{-5} Torr (vaporization temperature: 70–80 °C) to give mixtures of starting material **50**, ***E*-4-isothiocyanato-2-methyl-hexa-1,3,5-triene 52**, and **3-isothiocyanato-1-methyl-cyclohexa-1,3-diene 53**, which was purified by flash chromatography over neutral alumina using *n*-hexane, as pale yellow oil (the color is not stable), see Table 3.

Data of **53**



53

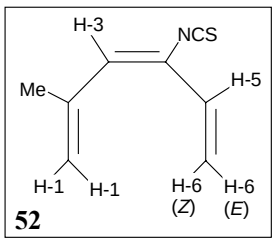
IR (neat): 2050 (NCS) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.82 (s, 3H, Me), 2.09 (t, *J* = 9.6 Hz, 2H, H-6), 2.27 (td, *J* = 9.6 Hz, ^3J = 4.8 Hz, 2H, H-5), 5.54 (s, 1H, H-2), 5.58 (t, ^3J = 4.8 Hz, 1H, H-4).

^{13}C NMR ($CDCl_3$): δ = 22.24 (q, Me), 22.92 (t), 27.14 (t), 117.67 (d), 117.89 (d), 126.98 (s), 132.76 (s, NCS), 140.26 (s).

GC–MS; *m*/*z* (%): 151 [M^+] (93), 93 (75), 91 (81), 77 (100), 39 (97) (retention time: 16.15 min).

Data of **52**



52

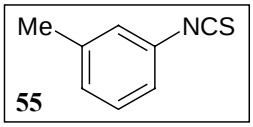
^{1}H NMR ($CDCl_3$): δ = 1.90 (s, 3H, Me), 5.03 (s, 1H, H-1), 5.18 (s, 1H, H-1), 5.32 (dd, 1H, ^3J = 16.7 Hz, ^2J = 2 Hz, *Z*-H-6), 5.61 (d, ^3J = 10.4 Hz, 1H, *E*-H-6), 6.09 (s, 1H, H-3), 6.80 (dd, 1H, ^3J = 16.7 Hz, ^3J = 10.4 Hz, H-5).

^{13}C NMR ($CDCl_3$): δ = 22.76 (q, Me), 117.43 (t), 120.22 (t), 128.53 (d), 130.44 (d), 138.71 (s), (two other quaternary carbons were not detected).

GC–MS; *m/z* (%): 151 [M^+] (29), 118 (71), 91 (60), 77 (79), 39 (100) (retention time: 14.55 min).

4.3.10 Oxidation of 3-Isothiocyanato-1-methyl-cyclohexa-1,3-diene 53

3-Isothiocyanato-1-methyl-cyclohexa-1,3-diene **53** (0.050 g, 0.33 mmol) was added dropwise to a stirred solution of DDQ (0.15 g, 0.66 mmol) in 5 ml of dichloromethane. After stirring for 3 h under reflux, the reaction mixture was cooled to room temperature, filtrated, and the solvent was evaporated to furnish the commercially available **1-isothiocyanato-3-methyl-benzene 55** (0.047 g, 0.315 mmol, 95%). Further purification was carried out by recondensation at 40 °C/ 10^{-2} Torr.



55

IR (neat): 2070 (NCS) cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 2.33 (s, 3H, Me), 7.00–7.25 (m, 4H, 4×Ar-H).
^{13}C NMR ($CDCl_3$): δ = 21.11 (q, Me), 122.67 (d), 126.24 (d), 128.16 (d), 129.22 (d), 130.89 (s), 134.73 (s, NCS), 139.63 (s).

4.3.11 Thermolysis of 2-Methyl-6-thiocyanato-hex-2-en-4-yne 50 in Solution

Heating diluted solutions of **50** in d_8–toluene in NMR tubes at 115 °C gave several products with different ratios as shown in Table 4.

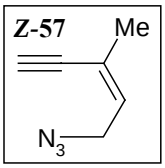
4.3.12 Synthesis of *Z/E*-1-Isothiocyanato-3-methyl-pent-2-en-4-yne 59

Z/E-1-Bromo-3-methyl-pent-2-en-4-yne **56**[39] (0.21 g, 1.32 mmol) was added slowly to a stirred solution of sodium azide (0.17 g, 2.64 mmol) in 20 ml of dry DMSO. After 1 h at room temperature, triphenylyphosphine (0.69 g, 2.64 mmol) dissolved in 2 ml of dry DMSO was added dropwise at 0 °C under nitrogen gas, and the reaction mixture was stirred at room temperature for 5 h. Finally, an excess amount of dry carbon disulfide (20 ml) was added at 0 °C under nitrogen gas. After stirring for 2 h at room temperature under nitrogen gas, water (20 ml) was added to the reaction mixture, and the product was extracted with diethyl ether (3×20 ml). The combined organic layers were washed with water (7×10 ml), dried ($MgSO_4$), and

concentrated. Recondensation of the crude product at 60 °C and 10^{-2} Torr afforded ***Z/E*-1-isothiocyanato-3-methyl-pent-2-en-4-yne 59** (with *Z*:*E* = 13:1) as colorless oil (0.15 g, 1.11 mmol, 84%).

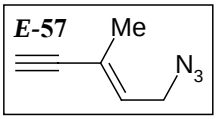
Data of Intermediates ***Z/E*-1-Azido-3-methyl-pent-2-en-4-yne 57**[40]

Data of ***Z*-57**[40]



^{1}H NMR (d_6-DMSO): δ = 1.82 (s, 3H, Me), 3.91 (d, ^3J = 7.5 Hz, 2H, CH_2), 4.36 (s, 1H, C≡CH), 5.90 (t, ^3J = 7.5 Hz, 1H, =CH).

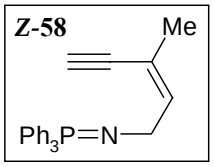
Data of ***E*-57**[40]



^{1}H NMR (d_6-DMSO): δ = 1.76 (s, 3H, Me), 3.95 (d, ^3J = 6.6 Hz, 2H, CH_2)
Not all signals could be detected, only two peaks were observed.

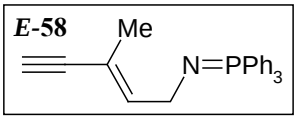
Data of Intermediates ***Z/E*-3-Methyl-1-(triphenylphosphoranylideneamino)-pent-2-en-4-yne 58**

Data of ***Z*-58**



^{1}H NMR (d_6-DMSO): δ = 1.62 (s, 3H, Me), 3.70 (dd, $^3J_{PH}$ = 20 Hz, ^3J = 6 Hz, 2H, CH_2), 3.95 (s, 1H, C≡CH), 5.90 (t, ^3J = 6 Hz, 1H, =CH).

Data of ***E*-58**

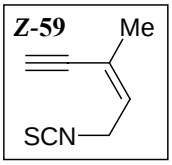


^{1}H NMR (d_6-DMSO): δ = 1.49 (s, 3H, Me)
Not all signals could be detected, only one peak was observed.

Data of ***Z/E*-1-Isothiocyanato-3-methyl-pent-2-en-4-yne 59**

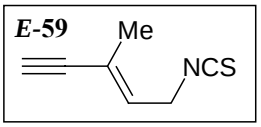
IR (neat): 3290, 2167, 2082 (NCS) cm^{-1} (for the mixture of two isomers).
Anal. Calcd for C_7H_7NS (137.20): C, 61.28; H, 5.14; N, 10.21; S, 23.37. **Found:** C, 61.11; H, 5.07; N, 9.91; S, 23.60 (for the mixture of two isomers).

Data of ***Z*-59**



^{1}H NMR ($CDCl_3$): δ = 1.91 (dt, ^4J = 1.5 Hz, ^5J = 1.2 Hz, 3H, Me), 3.25 (s, 1H, C≡CH), 4.29 (dq, ^3J = 6.9 Hz, ^5J = 1.2 Hz, 2H, CH_2), 5.80 (tqd, ^3J = 6.9 Hz, ^4J = 1.5 Hz, ^5J = 0.6 Hz, 1H, =CH).
^{13}C NMR ($CDCl_3$): δ = 22.63 (q, Me), 44.50 (t, C-1), 80.58 (s, C-4), 83.87 (d, C-5), 122.63 (s, C-3), 129.97 (d, C-2), 131.43 (s, NCS).
GC–MS; *m*/*z* (%): 137 [M^+] (6), 79 (92), 77 (100), 51 (47), 39 (35) (retention time: 13.40 min).

Data of ***E*-59**



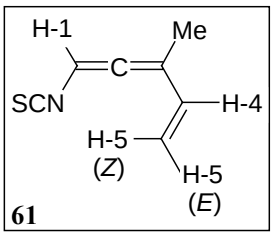
^{1}H NMR ($CDCl_3$): δ = 1.84 (dt, ^4J = 1.8 Hz, ^5J = 0.9 Hz, 3H, Me), 2.91 (s, 1H, C≡CH), 4.15 (d, ^3J = 6.9 Hz, 2H, CH_2), 5.96 (tqd, ^3J = 6.9 Hz, ^4J = 1.8 Hz, ^5J = 0.6 Hz, 1H, =CH).
^{13}C NMR ($CDCl_3$): δ = 17.40 (q, Me), 42.33 (t, C-1), 76.88 (d, C-5), 84.47 (s, C-4), 122.42 (s, C-3), 129.87 (d, C-2). The quaternary carbon of (N**C**S) was not detected.
GC–MS; *m*/*z* (%): 137 [M^+] (5), 79 (100), 77 (84), 51 (41), 39 (28) (retention time: 13.83 min).

4.3.13 FVP of *Z/E*-1-Isothiocyanato-3-methyl-pent-2-en-4-yne 59

Flash vacuum thermolysis of **59** (0.10 g, 0.66 mmol) was carried out at different temperatures (415, 400, 350, and 300 °C) and 10^{-2} Torr (vaporization temperature: 60–70 °C) to give

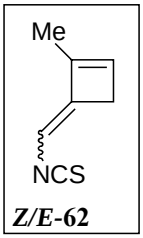
mixtures of starting material **59**, **1-isothiocyanato-3-methylpenta-1,2,4-triene 61**, and ***Z/E*-4-isothiocyanato-methylene-1-methyl-cyclobutene 62** (see Table 5).

Data for **61**



^{1}H NMR ($CDCl_3$): δ = 1.84 (m, 3H, Me), 5.23 (ddd, $^3J_{cis}$ = 10.5 Hz, ^2J = 1.5 Hz, ^6J = 0.9 Hz, 1H, *E*-H-5), 5.30 (ddd, $^3J_{trans}$ = 17.4 Hz, ^2J = 1.5 Hz, ^6J = 0.6 Hz, 1H, *Z*-H-5), 6.16 (m, 1H, H-1), 6.21 (ddd, $^3J_{trans}$ = 17.4 Hz, $^3J_{cis}$ = 10.5 Hz, ^5J = 0.9 Hz, 1H, H-4).
GC–MS; *m*/*z* (%): 137 [M^+] (42), 79 (40), 77 (100), 51 (56), 39 (53) (retention time: 14.10 min).

Data for ***Z/E*-62**

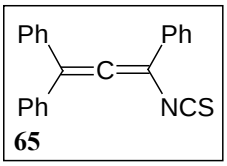


^{1}H NMR ($CDCl_3$): δ = 1.68 (m, 3H, Me), 1.90 (m, 3H, Me), 2.76 (m, 2H, CH_2), 2.89 (m, 2H, CH_2), 5.38 (m, 1H, =CH), 5.56 (m, 1H, =CH), 6.23 (m, 1H, =CH), 6.30 (m, 1H, =CH).
^{13}C NMR ($CDCl_3$): δ = 12.07 (q, Me), 13.52 (q, Me), 32.69 (t, C-3), 32.78 (t, C-3), 98.96 (d), 99.31 (d), 131.12 (s, NCS), 132.02 (s, NCS), 134.84 (d), 136.92 (d), 143.87 (s), 144.30 (s), 145.16 (s), 145.76 (s).
IR (neat): 2079 (br, NCS), 1672 cm^{-1} (for the mixture of two isomers).
GC–MS; *m*/*z* (%): 137 [M^+] (62), 79 (56), 77 (100), 51 (66), 39 (100). Both isomers ***Z*/*E*-62** have the same fragmentations with different retention times: 14.24 and 14.50 min, respectively.
Anal. Calcd for C_7H_7NS (137.20): C, 61.28; H, 5.14; N, 10.21; S, 23.37. **Found:** C, 60.90; H, 5.11; N, 10.03; S, 23.87 (for the mixture obtained at 400 °C).

4.3.14 Synthesis of 1,3,3-Triphenylallenyl Thiocyanate 65[43]

A three-necked flask equipped with a dropping funnel, stirrer, drying $CaCl_2$ tube and nitrogen gas inlet was charged with Ph_3P (0.58 g, 2.2 mmol) and dry MeCN (5 ml). Bromine (0.35 g, 2.2 mmol) was added dropwise to the solution at room temperature under nitrogen. When the

addition was completed, a solution of NH_4SCN (0.33 g, 4.4 mmol) in MeCN (5 ml) was added dropwise. To the resulting mixture, 1,1,3-triphenyl-prop-2-yn-1-ol **63** (0.60 g, 2.1 mmol), dissolved in 2 ml of dry MeCN, was then added dropwise. TLC of the reaction mixture showed immediate completion of the reaction after addition of the alcohol. The reaction mixture was filtered, and the filtrate extracted with MeCN. Evaporation of the solvent followed by column chromatography on silica gel using *n*-hexane and diethyl ether (7:3) gave **1,3,3-triphenylallenyl thiocyanate 65**[43] (0.58 g, 1.78 mmol, 85%). Recrystallization was done from diethyl ether and *n*-hexane.



65

M.p. = 104–105 °C (published[43] 115–116 °C).
IR ($CDCl_3$): 2157 (SCN), 1492, 1113 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 7.38–7.74 (m, 3×Ph).
^{13}C NMR ($CDCl_3$): δ = 98.41 (s), 110.22 (s, SCN), 117.78 (s), 126.67 (d), 128.80 (d), 128.89 (d), 128.92 (d), 129.06 (d), 129.08 (d), 131.78 (s), 134.09 (s), 206.92 (s).

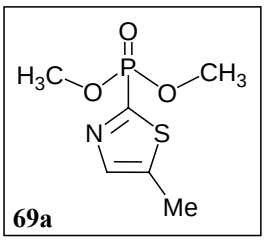
4.4 Succeeding Reactions of Allenyl ITCs 4a and 21 with Different Nucleophiles

4.4.1 Synthesis of Thiazoles Derivatives 69a–c; General Procedure I

Phosphites **68a–c** (1.0 equiv.) and 1-isothiocyanato-propa-1,2-diene **4a** 10% in dry THF (1.5 equiv.) were added to a suspension of K_2CO_3 (3.0 equiv.) in 20 ml of dry THF, after 5 h in the case of **68a**, 2 h in the case of **68b**, and 2.5 h in the case of **68c** at room temperature the solvent and excess allene **4a** were removed under vacuum to give substituted thiazoles **69a–c**.

4.4.1.1 Synthesis of Dimethyl 5-Methyl-thiazole-2-phosphonate 69a

Following general procedure **I**, compound **69a** was obtained (0.78 g, 3.77 mmol, 83%) as pale yellow oil. Purification was carried out by flash chromatography using ethyl acetate and CH_2Cl_2 (6:4).



IR ($CDCl_3$): 3006, 1448, 1254 (P=O), 1044 cm^{-1}.

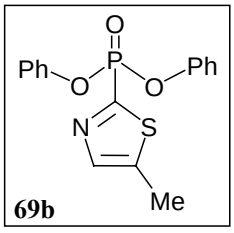
^{1}H NMR ($CDCl_3$): δ = 2.48 (d, ^4J = 1.2 Hz, 3H, Me), 3.76 (d, $^3J_{PH}$ = 11.4 Hz, 6H, 2×OMe), 7.70 (q, ^4J = 1.2 Hz, 1H, H-4).

^{13}C NMR ($CDCl_3$): δ = 11.61 (q, Me), 53.62 (q, d: $^2J_{PC}$ = 6.2 Hz, 2×OCH_3), 140.40 (s, C-5), 144.04 (d, d: $^3J_{PC}$ = 26.2 Hz, C-4), 153.20 (s, d: $^1J_{PC}$ = 245.8 Hz, C-2).

Anal. Calcd for $C_6H_{10}NO_3PS$ (207.19): C, 34.78; H, 4.86; N, 6.76; S, 15.48. **Found:** C, 34.48; H, 4.77; N, 6.62; S, 15.22.

4.4.1.2 Synthesis of Diphenyl 5-Methyl-thiazole-2-phosphonate 69b

Following general procedure **I**, thiazole **69b** was formed (0.64 g, 1.92 mmol, 90%) as colorless oil. Purification was carried out by flash column chromatography using THF and *n*-hexane (2:8).



IR ($CDCl_3$): 3076, 1491, 1275 (P=O), 1026 cm^{-1}.

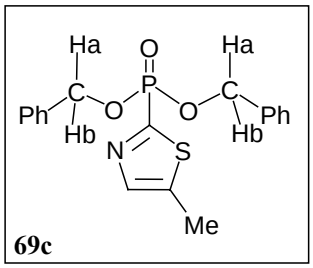
^{1}H NMR ($CDCl_3$): δ = 2.45 (d, ^4J = 1.2, 3H, Me), 7.08–7.26 (m, 10H, 2×Ph), 7.79 (q, ^4J = 1.2 Hz, 1H, H-4).

^{13}C NMR ($CDCl_3$): δ = 11.55 (q, Me), 120.35 (d, d: $^3J_{PC}$ = 4.6 Hz, 4×Ph_o), 125.29 (d, d: $^4J_{PC}$ = 1.1 Hz, 4×Ph_m), 129.50 (d, 2×Ph_p), 141.49 (s, C-5), 144.44 (d, d: $^3J_{PC}$ = 28.4 Hz, C-4), 149.59 (s, d: $^2J_{PC}$ = 7.4 Hz, 2×Ph_i), 152.02 (s, d: $^1J_{PC}$ = 256.6 Hz, C-2).

Anal. Calcd for $C_{16}H_{14}NO_3PS$ (331.33): C, 58.00; H, 4.26; N, 4.23; S, 9.68. **Found:** C, 57.60; H, 4.35; N, 4.30; S, 9.94.

4.4.1.3 Synthesis of Dibenzyl 5-Methyl-thiazole-2-phosphonate 69c

Following general procedure **I**, compound **69c** was furnished (0.60 g, 1.67 mmol, 88%) as white solid. Purification was carried out by flash column chromatography from THF and *n*-hexane (4:6). Crystallization can be executed using diethyl ether and *n*-hexane.



69c

M.p. = 45–46 °C

IR ($CDCl_3$): 3034, 1455, 1264 (P=O), 1001 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.47 (d, ^4J = 1.2 Hz, 3H, Me), 5.15 (dd, $^3J_{PH}$ = 12 Hz, ^2J = 8.1 Hz, 1H, CH_2), 5.16 (dd, $^3J_{PH}$ = 11.7 Hz, ^2J = 8.1 Hz, 1H, CH_2), 7.26–7.31 (m, 10H, 2×Ph), 7.74 (q, ^4J = 1.2 Hz, 1H, H-4).

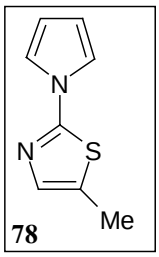
^{13}C NMR ($CDCl_3$): δ = 11.51 (q, Me), 68.52 (t, d: $^2J_{PC}$ = 5.6 Hz, 2×CH_2), 127.71 (d, 4×Ph), 128.20 (d, 2×Ph_p), 128.22 (d, 4×Ph), 135.19 (s, d: $^3J_{PC}$ = 6.8 Hz, 2×Ph_i), 140.22 (s, C-5), 143.94 (d, d: $^3J_{PC}$ = 26.8 Hz, C-4), 154.01 (s, d: $^1J_{PC}$ = 247.6 Hz, C-2).

Anal. Calcd for $C_{18}H_{18}NO_3PS$ (359.38): C, 60.16; H, 5.05; N, 3.90; S, 8.92. **Found:** C, 59.98; H, 5.29; N, 3.84; S, 9.03.

4.4.2 Synthesis of 5-Methyl-2-pyrrol-1-yl-thiazole 78 and 5-Methyl-2-(1*H*-pyrrol-2-yl)-thiazole 79

A solution of *n*-butyllithium in hexane (4.66 ml, 7.46 mmol, 1.6 M) was slowly added to a stirred solution of 1*H*-pyrrole (0.50 g, 7.46 mmol) **76** in 8 ml of dry THF at –78 °C. The temperature of the reaction mixture was slowly raised to room temperature and stirring continued for 5 h at room temperature. The mixture was cooled to –40 °C and 1-isothiocyanato-propa-1,2-diene (**4a**) 10% in dry THF (1.09 g, 11.24 mmol) was added over a period of 5 min under nitrogen gas. The reaction mixture was allowed to slowly warm up to room temperature and stirred overnight at that temperature. Diethyl ether (30 ml) was added, and the mixture was then washed with saturated ammonium chloride solution (25 ml). The organic layer was separated, and the aqueous layer was extracted with diethyl ether (3×10 ml). The organic extracts were combined, dried ($MgSO_4$), concentrated, and the crude compounds were separated by flash chromatography using diethyl ether and *n*-hexane (3:7) to give **5-methyl-2-pyrrol-1-yl-thiazole 78** as a white solid (0.73 g, 4.45 mmol, 60%) and then **5-methyl-2-(1*H*-pyrrol-2-yl)-thiazole 79** as a white solid (0.19 g, 1.16 mmol, 16%). The products were recrystallized either from *n*-pentane (compound **78**) or from diethyl ether and *n*-hexane (compound **79**).

Data of **78**



M.p. = 37.5–38.5 °C

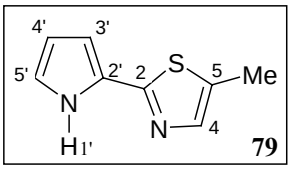
IR ($CDCl_3$): 1550, 1516, 1347, 1065 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.40 (d, ^4J = 1.2 Hz, 3H, Me), 6.32 (dd, J = 2.4 Hz, J = 2.1 Hz, 2H, =CH), 7.11 (q, ^4J = 1.2 Hz, 1H, H-4), 7.28 (dd, J = 2.4 Hz, J = 2.1 Hz, 2H, =CH).

^{13}C NMR ($CDCl_3$): δ = 11.78 (q, Me), 111.49 (d), 119.24 (d), 128.38 (s, C-5), 136.98 (d, C-4), 159.30 (s, C-2).

Anal. Calcd for $C_8H_8N_2S$ (164.23): C, 58.51; H, 4.91; N, 17.06; S, 19.52. **Found:** C, 58.49; H, 4.82; N, 17.11; S, 19.61.

Data of **79**



M.p. = 115–116 °C

IR ($CDCl_3$): 3466, 1576, 1429, 1089 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.45 (d, ^4J = 1.2 Hz, 3H, Me), 6.24 (ddd, $^3J_{4'–3'}$ = 3.7 Hz, $^3J_{4'–5'}$ = 2.7 Hz, $^4J_{4'–1'}$ = 2.6 Hz, 1H, H-4'), 6.61 (ddd, $^3J_{3'–4'}$ = 3.7 Hz, 1H, $^4J_{3'–1'}$ = 2.6 Hz, $^4J_{3'–5'}$ = 1.4 Hz, H-3'), 6.88 (ddd, $^3J_{5'–1'}$ = 2.7 Hz, 1H, $^3J_{5'–4'}$ = 2.7 Hz, $^4J_{5'–3'}$ = 1.4 Hz, H-5'), 7.29 (q, ^4J = 1.2 Hz, 1H, H-4), 10.51 (br s, 1H, NH).

^{13}C NMR ($CDCl_3$): δ = 11.87 (q, Me), 109.40 (d), 109.90 (d), 120.34 (d), 126.52 (s), 131.07 (s), 139.43 (d, C-4), 159.87 (s, C-2).

Anal. Calcd for $C_8H_8N_2S$ (164.23): C, 58.51; H, 4.91; N, 17.06; S, 19.52. **Found:** C, 58.60; H, 4.94; N, 17.06; S, 19.71.

4.4.3 Synthesis of 5-Methyl-2-(2-thienyl)-thiazole 82 and 5-Methyl-2'-(2-thienyl)-2,5'-methylenebisthiazole 84

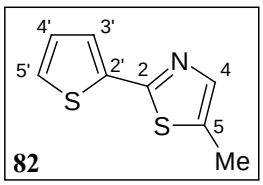
- Method **A**

By this method, two compounds **82**[60] and **84** were obtained.

The procedure

To a stirred solution of thien-2-ylmagnesium bromide[59] (calculated to be 0.50 g, 2.67 mmol, made from 0.66 g of Mg and 0.44 g of 2-bromothiophene) **80** in 20 ml of dry diethyl ether at –7 °C, 1-isothiocyanato-propa-1,2-diene (**4a**) 10% in dry diethyl ether (0.39 g, 4.02 mmol) was slowly added. The temperature of the reaction mixture was slowly raised to 0 °C and stirring continued for 20 min at this temperature. Diethyl ether (50 ml), was added and the mixture was then washed with saturated aqueous ammonium chloride (20 ml). The organic layer was separated, and the aqueous layer was extracted with diethyl ether (3×20 ml). The organic extracts were combined, dried ($MgSO_4$), concentrated, and the crude products were separated by flash chromatography using diethyl ether and *n*-hexane (3:7) to yield **5-methyl-2-(2-thienyl)-thiazole 82**[60] as pale yellow oil (0.13 g, 0.718 mmol, 27%) and then **5-methyl-2'-(2-thienyl)-2,5'-methylenebisthiazole 84** as pale yellow oil (0.12 g, 0.432 mmol, 16%).

Data of **82**[60]

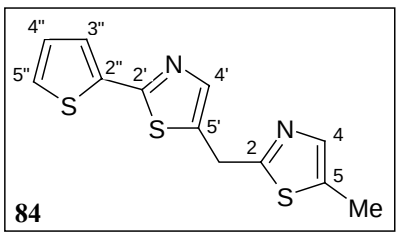


82

^{1}H NMR ($CDCl_3$): δ = 2.47 (d, ^4J = 1.2 Hz, 3H, Me), 7.03 (dd, $^3J_{4'–5'}$ = 5.1 Hz, $^3J_{4'–3'}$ = 3.6 Hz, 1H, H-4'), 7.33 (dd, $^3J_{5'–4'}$ = 5.1 Hz, $^4J_{5'–3'}$ = 1.2 Hz, 1H, H-5'), 7.39 (q, ^4J = 1.2 Hz, 1H, H-4), 7.41 (dd, $^3J_{3'–4'}$ = 3.6 Hz, $^4J_{3'–5'}$ = 1.2 Hz, 1H, H-3').

^{13}C NMR ($CDCl_3$): δ = 11.96 (q, Me), 125.45 (d), 126.97 (d), 127.69 (d), 133.21 (s), 137.67 (s), 140.85 (d, C-4), 160.33 (s, C-2).

Data of **84**



84

IR ($CDCl_3$): 1602, 1414, 1143 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.41 (d, ^4J = 1.2 Hz, 3H, Me), 4.44 (d, ^4J = 0.9 Hz, 2H, CH_2), 7.03 (dd, $^3J_{4"–5"}$ = 5.1 Hz, $^3J_{4"–3"}$ = 3.9 Hz, 1H, H-4"), 7.34 (q, ^4J = 1.2 Hz, 1H, H-4), 7.35 (dd, $^3J_{5"–4"}$ = 5.1 Hz, $^4J_{5"–3"}$ = 1.2 Hz, 1H, H-5"), 7.42 (dd, $^3J_{3"–4"}$ = 3.9 Hz, $^4J_{3"–5"}$ = 1.2 Hz, 1H, H-3"), 7.57 (t, ^4J = 0.9 Hz, 1H, H-4').

^{13}C NMR ($CDCl_3$): δ = 11.88 (q, Me), 30.94 (t) 126.38 (d), 127.49 (d), 127.75 (d), 133.91 (s), 134.34 (s) 137.27 (s), 140.13 (d), 141.48 (d), 161.97 (s), 165.87 (s).
ESI–MS ($C_{12}H_{10}N_2S_3$). **Calculated:** 279.0079 $[M+H]^+$. **Found:** 279.0124.

- Method **B**

Only compound **82**[60] was obtained by this method.

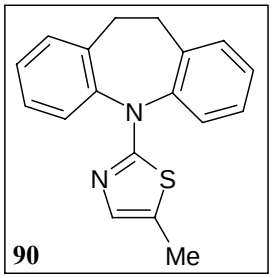
The procedure

To a solution of thien-2-yllithium[61] (calculated to be 0.50 g, 5.56 mmol, made from 0.47 g of thiophene and 2.24 ml of *n*-BuLi in hexane 2.5 M) **86** in 40 ml of dry THF at –90 °C, 1-isothiocyanato-propa-1,2-diene (**4a**) 10% in dry THF (0.80 g, 8.25 mmol) was slowly added. The temperature of the reaction mixture was slowly raised to –80 °C and stirring continued for 30 min at this temperature. Diethyl ether (20 ml) was added, and the mixture was then washed with saturated aqueous ammonium chloride (25 ml). The organic layer was separated, and the aqueous layer was extracted with diethyl ether (3×10 ml). The organic extracts were combined, dried ($MgSO_4$), concentrated, and the crude compound was purified by flash chromatography using diethyl ether and *n*-hexane (2:8) to afford **5-methyl-2-(2-thienyl)-thiazole 82**[60] as pale yellow oil (0.10 g, 0.525 mmol, 10%).

4.4.4 Synthesis of 5-(5-Methyl-thiazol-2-yl)-10,11-dihydro-5*H*-dibenzo[b,f]azepine 90

10,11-Dihydro-5*H*-dibenzo[b,f]azepine (0.50 g, 2.56 mmol) **88** in 2 ml of dry THF was added dropwise to a solution of isopropylmagnesium bromide (calculated to be 0.377 g, 2.56 mmol, prepared from 0.0622 g of Mg and 0.315 g of isopropyl bromide) in 4 ml of dry THF. The mixture was stirred for 2 h at room temperature, and the 1-isothiocyanato-propa-1,2-diene (**4a**) 10% in dry THF (0.372 g, 3.84 mmol) was added over a period of 5 min under nitrogen gas at 0 °C. After 3 h stirring at room temperature, diethyl ether (15 ml) was added, and the mixture was then washed with saturated aqueous ammonium chloride (20 ml). The organic layer was separated, and the aqueous layer was extracted with diethyl ether (3×10 ml). The organic extracts were combined, dried ($MgSO_4$), concentrated, and the residue was purified by flash

chromatography using diethyl ether and *n*-hexane (1:1) to furnish **5-(5-methyl-thiazol-2-yl)-10,11-dihydro-5*H*-dibenzo-[b,f]azepine 90** as pale yellow-green solid (0.261 g, 0.893 mmol, 35%). Crystallization was done using diethyl ether and *n*-hexane.



90

M.p. = 119–121 °C

IR ($CDCl_3$): 1504, 1446, 1324, 1150 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.23 (d, ^4J = 1.2 Hz, 3H, Me), 3.10 (s, 4H, 2×CH_2), 6.83 (q, ^4J = 1.2 Hz, 1H, H-4'), 7.24–7.59 (m, 8H, 8×Ar-H).

^{13}C NMR ($CDCl_3$): δ = 11.73 (q, Me), 30.79 (t, 2×CH_2), 122.08 (s, C-5'), 127.13 (d, 2C), 127.83 (d, 2C), 128.64 (d, 2C), 130.51 (d, 2C), 136.38 (d, C-4'), 136.97 (s, 2C), 142.74 (s, 2C), 169.59 (s, C-2').

Anal. Calcd for $C_{18}H_{16}N_2S$ (292.40): C, 73.94; H, 5.52; N, 9.58; S, 10.97. **Found:** C, 73.40; H, 5.54; N, 9.60; S, 10.61.

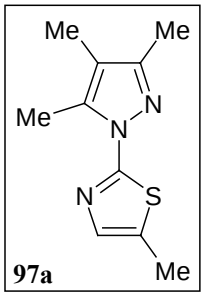
4.4.5 Synthesis of Thiazole Derivatives; General Procedure II

Allenyl ITC **4a** (10% in dry THF, 1.5 equiv.) or **21** (10% in dry THF, 1.50 equiv.) was added to azoles **94a**–**c**, **95a**,**b**, and **96** (1.00 equiv.) dissolved in 5 ml of a dry appropriate solvent (Table 7). After the reaction completed, the solvent was removed in vacuo, and the crude reaction mixtures were separated by flash chromatography diethyl ether and *n*-hexane (2:8) for **97a**,**e** and **98a**,**e**, ethyl acetate and CH_2Cl_2 (3:7) for **97c**,**d**, ethyl acetate and *n*-hexane (3:7) for **97b**,**f** and **98b**,**f**, ethyl acetate and CH_2Cl_2 (4:6) for **97i** and **98i**, acetone and *n*-hexane (4:6) for **97g** and **98g** as well as acetone and *n*-hexane (2:8) for **97h**. Upon separation by flash chromatography, the nonaromatic product was eluted before the aromatic one in all cases.

4.4.5.1 Synthesis of 5-Methyl-2-(3,4,5-trimethyl-pyrazol-1-yl)-thiazole 97a and 5-Methyl-ene-2-(3,4,5-trimethyl-pyrazol-1-yl)-4,5-dihydro-thiazole 98a

Following the general procedure **II**, thiazoles **97a** (0.62 g, 3.00 mmol, 66%) and **98a** (0.21 g, 1.00 mmol, 22%) were yielded as white solid (recrystallization from *n*-hexane)

Data of **97a**



M.p. = 82–83 °C.

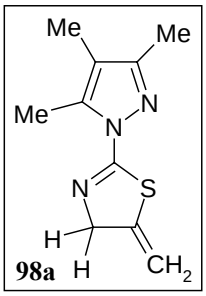
IR ($CDCl_3$): 1595 (C=C), 1449 (C=N), 1277 (S–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.94 (s, 3H, Me), 2.21 (s, 3H, Me), 2.40 (d, ^4J = 1.3 Hz, 3H, Me), 2.55 (s, 3H, Me), 7.12 (q, ^4J = 1.3 Hz, 1H, H-4).

^{13}C NMR ($CDCl_3$): δ = 7.81 (q, Me), 11.77 (q, Me), 11.81 (q, Me), 12.02 (q, Me), 115.46 (s), 129.29 (s), 136.87 (d, C-4), 137.45 (s), 150.57 (s), 161.01 (s).

Anal. Calcd for $C_{10}H_{13}N_3S$ (207.29): C, 57.94; H, 6.32; N, 20.27; S, 15.47. **Found:** C, 57.73; H, 6.35; N, 19.96; S, 16.02.

Data of **98a**



M.p. = 72–73 °C.

IR ($CDCl_3$): 1619 (C=C), 1432 (C=N), 1275 (S–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.91 (s, 3H, Me), 2.18 (s, 3H, Me), 2.46 (s, 3H, Me), 5.01 (t, ^4J = 2.4 Hz, 2H), 5.21 (t, ^4J = 2.4 Hz, 2H).

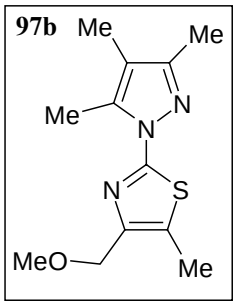
^{13}C NMR ($CDCl_3$): δ = 7.73 (q, Me), 12.05 (q, Me), 12.10 (q, Me), 68.49 (t, C-4), 102.86 (t, $=CH_2$), 116.44 (s), 138.51 (s), 146.89 (s), 151.16 (s), 156.85 (s).

Anal. Calcd for $C_{10}H_{13}N_3S$ (207.29): C, 57.94; H, 6.32; N, 20.27; S, 15.47. **Found:** C, 57.93; H, 6.25; N, 20.22; S, 15.59.

4.4.5.2 Synthesis of 4-Methoxymethyl-5-methyl-2-(3,4,5-trimethyl-pyrazol-1-yl)-thiazole 97b and 4-Methoxymethyl-5-methylene-2-(3,4,5-trimethyl-pyrazol-1-yl)-4,5-dihydro-thiazole 98b

Following the general procedure **II**, thiazoles **97b** (0.44 g, 1.75 mmol, 39%) and **98b** (0.52 g, 2.07 mmol, 46%) were obtained as white solid (recrystallization from *n*-hexane) and colorless oil, respectively.

Data of **97b**



M.p. = 79–80 °C.

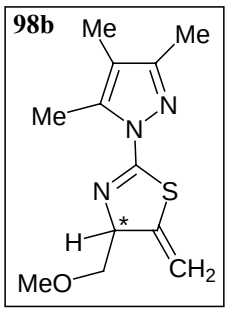
IR ($CDCl_3$): 1595 (C=C),1431 (C=N), 1363 (S–C), 1084 (C–O–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.89 (s, 3H, Me), 2.17 (s, 3H, Me), 2.37 (s, 3H, Me), 2.53 (s, 3H, Me), 3.38 (s, 3H, OMe), 4.39 (s, 2H, OCH_2).

^{13}C NMR ($CDCl_3$): δ = 7.67 (q, Me), 10.70 (q, Me), 11.67 (q, Me), 11.89 (q, Me), 57.94 (q, OMe), 67.55 (t, OCH_2), 115.26 (s), 127.18 (s), 137.39 (s), 145.08 (s), 150.40 (s), 158.68 (s).

Anal. Calcd for $C_{12}H_{17}N_3OS$ (251.35): C, 57.34; H, 6.82; N, 16.72; S, 12.67. **Found:** C, 57.16; H, 6.66; N, 16.81; S, 12.85.

Data of **98b**



IR ($CDCl_3$): 1638 (C=C), 1431 (C=N), 1363 (S–C), 1120 (C–O–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.84 (s, 3H, Me), 2.11 (s, 3H, Me), 2.42 (s, 3H, Me), 3.37 (s, 3H, OMe), 3.50 (m, 2H, OCH_2, diastereotopic protons), 5.12 (m, 1H), 5.24 (m, 2H).

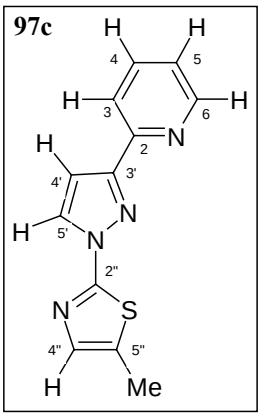
^{13}C NMR ($CDCl_3$): δ = 7.42 (q, Me), 11.74 (q, Me), 11.94 (q, Me), 59.15 (q, OMe), 75.91 (t, OCH_2), 78.41 (d, C-4), 104.28 (t, $=CH_2$), 116.23 (s), 138.37 (s), 147.70 (s), 150.94 (s), 156.12 (s).

Anal. Calcd for $C_{12}H_{17}N_3OS$ (251.35): C, 57.34; H, 6.82; N, 16.72; S, 12.67. **Found:** C, 57.19; H, 6.83; N, 16.76; S, 13.03.

4.4.5.3 Synthesis of 2-[1-(5-Methyl-thiazol-2-yl)-1*H*-pyrazol-3-yl]-pyridine 97c

Following the general procedure **II**, thiazole **97c** (0.45 g, 1.88 mmol, 91%) was generated as white solid (recrystallization from diethyl ether).

Data of **97c**



M.p. = 124–125 °C.

IR ($CDCl_3$): 1550 (C=C), 1422 (C=N), 1261 (S–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.45 (d, ^4J = 1.3, 3H, Me), 7.10 (d, ^3J = 3.0 Hz, 1H, H-4'), 7.18 (q, ^4J = 1.3 Hz, 1H, H-4''), 7.24 (ddd, ^3J = 7.5 Hz, ^3J = 4.8 Hz, ^4J = 1.2 Hz, 1H, H-5), 7.74 (ddd, ^3J = 7.8 Hz, ^3J = 7.5 Hz, ^4J = 1.7 Hz, 1H, H-4), 8.07 (ddd, ^3J = 7.8 Hz, ^4J = 1.2 Hz, ^5J = 1.0 Hz, 1H, H-3), 8.31 (d, ^3J = 3.0 Hz, 1H, H-5'), 8.64 (ddd, ^3J = 4.8 Hz, ^4J = 1.7 Hz, ^5J = 1.0 Hz, 1H, H-6).

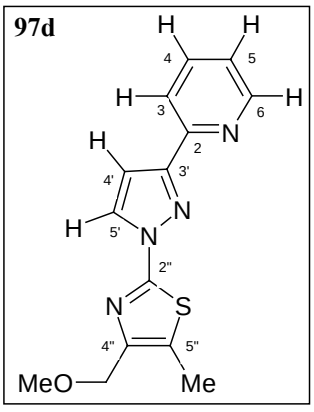
^{13}C NMR ($CDCl_3$): δ = 11.99 (q, 5''-Me), 107.14 (d, C-4'), 120.51 (d, C-3), 123.13 (d, C-5), 128.22 (d, C-5'), 130.79 (s, C-5''), 136.57 (d, C-4), 137.17 (d, C-4''), 149.40 (d, C-6), 151.00 (s), 154.21 (s), 159.43 (s), assignments by C–H shift correlation.

Anal. Calcd for $C_{12}H_{10}N_4S$ (242.30): C, 59.48; H, 4.14; N, 22.93; S, 13.38. **Found:** C, 59.15; H, 4.15; N, 23.12; S, 13.23.

4.4.5.4 Synthesis of 2-[1-(4-Methoxymethyl-5-methyl-thiazol-2-yl)-1*H*-pyrazol-3-yl]-pyridine 97d

Following the general procedure **II**, thiazole **97d** (0.52 g, 1.82 mmol, 88%) was obtained as white solid (recrystallization from *n*-hexane).

Data of **97d**



M.p. = 108–109 °C.

IR ($CDCl_3$): 1545 (C=C), 1404 (C=N), 1366 (S–C), 1086 (C–O–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.46 (s, 3H, Me), 3.44 (s, 3H, OMe), 4.44 (s, 2H, OCH_2), 7.10 (d, ^3J = 2.6 Hz, 1H, H-4'), 7.25 (ddd, ^3J = 7.7 Hz, ^3J = 4.9 Hz, ^4J = 1.3 Hz, 1H, H-5), 7.75 (ddd, ^3J = 7.9 Hz, ^3J = 7.7 Hz, ^4J = 1.9 Hz, 1H, H-4), 8.06 (ddd, ^3J = 7.9 Hz, ^4J = 1.3 Hz, ^5J =

1.0 Hz, 1H, H-3), 8.36 (d, ^3J = 2.6 Hz, 1H, H-5'), 8.64 (ddd, ^3J = 4.9 Hz, ^4J = 1.9 Hz, ^5J = 1.0 Hz, 1H, H-6).

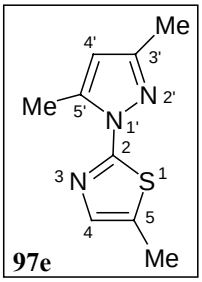
^{13}C NMR ($CDCl_3$): δ = 11.14 (q, 5''-Me), 58.31 (q, OMe), 67.43 (t, OCH_2), 107.12 (d, C-4'), 120.56 (d, C-3), 123.16 (d, C-5), 128.48 (d, C-5'), 128.68 (s), 136.64 (d, C-4), 145.47 (s), 149.37 (d, C-6), 150.96 (s), 154.20 (s), 157.58 (s), assignments by C–H shift correlation.

Anal. Calcd for $C_{14}H_{14}N_4OS$ (286.36): C, 58.72; H, 4.93; N, 19.57; S, 11.20. **Found:** C, 58.49; H, 4.90; N, 19.42; S, 11.31.

4.4.5.5 Synthesis of 2-(3,5-Dimethyl-pyrazol-1-yl)-5-methyl-thiazole 97e and 2-(3,5-Dimethyl-pyrazol-1-yl)-5-methylene-4,5-dihydro-thiazole 98e

Following the general procedure **II**, thiazoles **97e** (0.50 g, 2.58 mmol, 49%) and **98e** (0.33 g, 1.70 mmol, 33%) were afforded as yellow oil and white solid (recrystallization from *n*-hexane), respectively.

Data of **97e**



97e

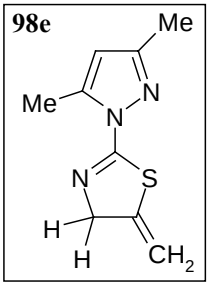
IR ($CDCl_3$): 1573 (C=C), 1442 (C=N), 1262 (S–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.26 (s, 3H, Me), 2.41 (d, ^4J = 1.2 Hz, 3H, Me-5), 2.61 (s, 3H, Me), 5.95 (s, 1H, H-4'), 7.13 (q, ^4J = 1.2 Hz, 1H, H-4).

^{13}C NMR ($CDCl_3$): δ = 11.77 (q, Me), 13.45 (q, Me), 13.50 (q, Me), 109.06 (d, C-4'), 129.78 (s), 137.01 (d, C-4), 141.14 (s), 150.96 (s), 160.56 (s).

Anal. Calcd for $C_9H_{11}N_3S$ (193.27): C, 55.93; H, 5.74; N, 21.74; S, 16.59. **Found:** C, 55.77; H, 5.83; N, 21.55; S, 17.64.

Data of **98e**



M.p. = 75–76 °C.

IR ($CDCl_3$): 1573 (C=C), 1440 (C=N), 1265 (S–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.23 (s, 3H, Me), 2.53 (s, 3H, Me), 5.02 (t, ^4J = 2.7 Hz, 2H), 5.22 (m, 2H), 5.95 (s, 1H, H-4').

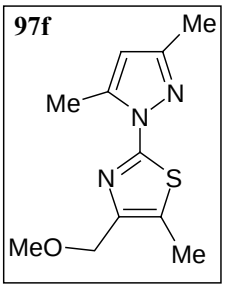
^{13}C NMR ($CDCl_3$): δ = 13.52 (q, Me), 13.83 (q, Me), 68.55 (t, C-4), 103.11 (t, $=CH_2$), 110.00 (d, C-4'), 142.55 (s), 146.89 (s), 151.35 (s), 156.69 (s).

Anal. Calcd for $C_9H_{11}N_3S$ (193.27): C, 55.93; H, 5.74; N, 21.74; S, 16.59. **Found:** C, 55.91; H, 5.76; N, 21.58; S, 16.98.

4.4.5.6 Synthesis of 2-(3,5-Dimethyl-pyrazol-1-yl)-4-methoxymethyl-5-methyl-thiazole 97f and 2-(3,5-Dimethyl-pyrazol-1-yl)-4-methoxymethyl-5-methylene-4,5-dihydro-thiazole 98f

Following the general procedure **II**, thiazoles **97f** (0.61 g, 2.57 mmol, 50%) and **98f** (0.37 g, 1.56 mmol, 30%) were obtained as colorless oils.

Data of **97f**



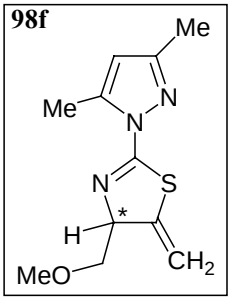
IR ($CDCl_3$): 1573 (C=C), 1412 (C=N), 1365 (S–C), 1083 (C–O–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.25 (s, 3H, Me), 2.42 (s, 3H, Me), 2.63 (s, 3H, Me), 3.41 (s, 3H, OMe), 4.43 (s, 2H, OCH_2), 5.94 (s, 1H, H-4').

^{13}C NMR ($CDCl_3$): δ = 10.44 (q, Me), 13.15 (q, Me), 13.16 (q, Me), 57.70 (q, OMe), 67.30 (t, OCH_2), 108.71 (d, C-4'), 127.44 (s), 140.87 (s), 145.09 (s), 150.54 (s), 158.06 (s).

Anal. Calcd for $C_{11}H_{15}N_3OS$ (237.33): C, 55.67; H, 6.37; N, 17.71; S, 13.51. **Found:** C, 55.47; H, 6.37; N, 17.58; S, 13.68.

Data of **98f**



IR ($CDCl_3$): 1573 (C=C), 1412 (C=N), 1365 (S–C), 1084 (C–O–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.22 (s, 3H, Me), 2.54 (s, 3H, Me), 3.42 (s, 3H, OMe), 3.62 (m, 2H, OCH_2, diastereotopic protons), 5.19 (m, 1H), 5.31 (m, 2H), 5.94 (s, 1H, H-4').

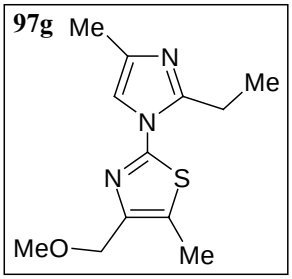
^{13}C NMR ($CDCl_3$): δ = 13.50 (q, Me), 13.92 (q, Me), 59.44 (q, OMe), 76.02 (t, OCH_2), 78.75 (d, C-4), 104.81 (t, $=CH_2$), 110.03 (d, C-4'), 142.74 (s), 147.79 (s), 151.47 (s), 156.23 (s).

Anal. Calcd for $C_{11}H_{15}N_3OS$ (237.33): C, 55.67; H, 6.37; N, 17.71; S, 13.51. **Found:** C, 55.37; H, 6.31; N, 17.59; S, 13.91.

4.4.5.7 Synthesis of 2-(2-Ethyl-4-methyl-imidazol-1-yl)-4-methoxymethyl-5-methyl-thiazole 97g and 2-(2-Ethyl-4-methyl-imidazol-1-yl)-4-methoxymethyl-5-methylene-4,5-dihydro-thiazole 98g

Following the general procedure **II**, thiazoles **97g** (0.90 g, 3.59 mmol, 79%) and **98g** (0.03 g, 0.136 mmol, 3%) were furnished as orange and yellow oil, respectively.

Data of **97g**



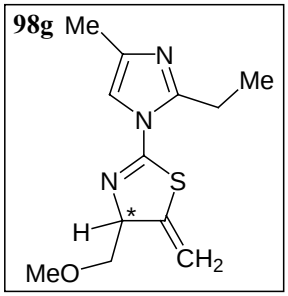
IR ($CDCl_3$): 1588 (C=C), 1401 (C=N), 1334 (S–C), 1070 (C–O–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.21 (t, ^3J = 7.5 Hz, 3H, CH_2Me), 2.10 (s, 3H, Me-5), 2.36 (d, ^4J = 1.2 Hz, 3H, Me-4'), 2.85 (q, ^3J = 7.5 Hz, 2H, CH_2Me), 3.32 (s, 3H, OMe), 4.36 (s, 2H, OCH_2), 6.86 (q, ^4J = 1.2 Hz, 1H, H-5').

^{13}C NMR ($CDCl_3$): δ = 10.74 (q, Me), 11.73 (q, Me), 13.12 (q, Me), 21.54 (t, CH_2CH_3), 58.02 (q, OMe), 67.16 (t, OCH_2), 115.53 (d, C-5'), 129.51 (s), 136.92 (s), 145.82 (s), 149.07 (s), 153.40 (s).

Anal. Calcd for $C_{12}H_{17}N_3OS$ (251.35): C, 57.34; H, 6.82; N, 16.72; S, 12.76. **Found:** C, 57.12; H, 6.63; N, 16.50; S, 12.69.

Data of **98g**



IR ($CDCl_3$): 1640 (C=C), 1401 (C=N), 1292 (S–C), 1072 (C–O–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.26 (t, ^3J = 7.5 Hz, 3H, CH_2Me), 2.13 (d, ^4J = 1.2 Hz, 3H, Me-4'), 2.97 (m, 2H, CH_2Me, diastereotopic protons), 3.38 (s, 3H, OMe), 3.62 (m, 2H, OCH_2, diastereotopic protons), 5.14 (m,

1H), 5.34 (m, 2H), 6.75 (q, ^4J = 1.2 Hz, 1H, H-5').

^{13}C NMR ($CDCl_3$): δ = 11.80 (q, Me), 13.30 (q, Me), 22.29 (t, CH_2CH_3), 59.44 (q, OMe), 75.46 (t, OCH_2), 78.42 (d, C-4), 106.23 (t, $=CH_2$), 115.19 (d, C-5'), 137.21 (s), 147.41 (s), 150.91 (s), 151.65 (s).

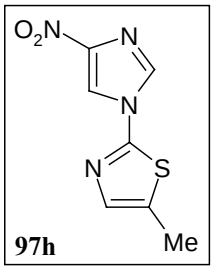
ESI–MS ($C_{12}H_{17}N_3OS$). **Calculated:** for $[M+H]^+$ 252.1165. **Found:** 252.1184.

4.4.5.8 Synthesis of 5-Methyl-2-(4-nitro-imidazol-1-yl)-thiazole 97h

Following the general procedure **II**, thiazoles **97h** (0.63 g, 3.00 mmol, 68%) was obtained as white solid (recrystallization from diethyl ether).

Data of **97h**

M.p. = 148–150 °C.



97h

IR ($CDCl_3$): 1554 (C=C), 1517 (NO_2), 1401 (C=N), 1228 (S–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.52 (d, ^4J = 1.5 Hz, 3H, Me), 7.32 (q, ^4J = 1.5 Hz, 1H, H-4), 8.05 (d, ^4J = 1.5 Hz, 1H, H-2' or H-5'), 8.25 (d, ^4J = 1.5 Hz, 1H, H-5' or H-2').

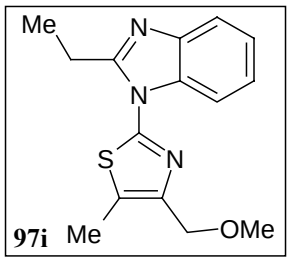
^{13}C NMR ($CDCl_3$): δ = 12.07 (q, Me), 116.85 (d), 133.56 (s), 133.70 (d), 138.37 (d), 148.62 (s), 152.77 (s).

Anal. Calcd for $C_7H_6N_4O_2S$ (242.22): C, 39.99; H, 2.88; N, 26.65; S, 15.25. **Found:** C, 40.23; H, 2.86; N, 26.58; S, 15.26.

4.4.5.9 Synthesis of 2-Ethyl-1-(4-methoxymethyl-5-methyl-thiazol-2-yl)-1*H*-benzimidazole 97i and 2-Ethyl-1-(4-methoxymethyl-5-methylene-4,5-dihydro-thiazol-2-yl)-1*H*-benzimidazole 98i

Following the general procedure **II**, thiazoles **97i** (0.60 g, 2.09 mmol, 76%) and **98i** (0.13 g, 0.45 mmol, 17%) were yielded as yellow oils.

Data of **97i**



97i

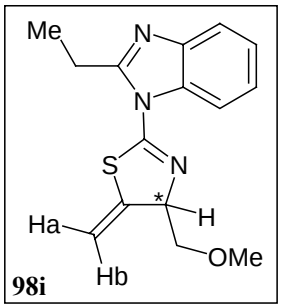
IR ($CDCl_3$): 1613 (C=C), 1453 (C=N), 1364 (S–C), 1075 (C–O–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.30 (t, ^3J = 7.8 Hz, 3H, CH_2Me), 2.39 (s, 3H, Me-5'), 2.95 (q, ^3J = 7.8 Hz, 2H, CH_2Me), 3.32 (s, 3H, OMe), 4.41 (s, 2H, OCH_2), 7.14 (m, 2H, Ar-H), 7.45 (m, 1H, Ar-H), 7.64 (m, 1H, Ar-H).

^{13}C NMR ($CDCl_3$): δ = 10.86 (q, Me), 11.20 (q, Me), 21.56 (t, CH_2Me), 57.96 (q, OMe), 67.05 (t, OCH_2), 110.19 (d), 118.94 (d), 122.80 (d), 123.00 (d), 131.86 (s), 134.72 (s), 141.95 (s), 146.30 (s), 151.45 (s), 155.78 (s).

Anal. Calcd for $C_{15}H_{17}N_3OS$ (287.38): C, 62.69; H, 5.96; N, 14.62; S, 11.16. **Found:** C, 62.50; H, 5.78; N, 14.60; S, 11.62.

Data of **98i**



98i

IR ($CDCl_3$): 1615 (C=C), 1456 (C=N), 1364 (S–C), 1073 (C–O–C) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.43 (t, ^3J = 7.8 Hz, 3H, CH_2Me), 3.14 (m, 2H, CH_2Me, diastereotopic protons), 3.41 (s, 3H, OMe), 3.75 (m, 2H, OCH_2, diastereotopic protons), 5.27 (m, 1H, H-4'), 5.41 (dd, ^4J = 2.5 Hz, ^2J = 2.1 Hz, 1H, C=CH_2), 5.47 (dd, ^4J = 2.3 Hz, ^2J = 2.1 Hz, 1H, C=CH_2), 7.27 (m, 2H, 2×Ar-H), 7.72 (m, 2H, 2×Ar-H).

^{13}C NMR ($CDCl_3$): δ = 11.61 (q, CH_2Me), 22.59 (t, CH_2Me), 59.30 (q, OMe), 75.31 (t, OCH_2), 77.14 (d, C-4'), 106.54 (t, =CH_2), 112.10 (d), 119.29 (d), 123.41 (d, 2×Ar-C), 133.82 (s), 142.14 (s), 147.31 (s), 152.22 (s), 156.08 (s).

Anal. Calcd for $C_{15}H_{17}N_3OS$ (287.38): C, 62.69; H, 5.96; N, 14.62; S, 11.16. **Found:** C, 62.14; H, 6.04; N, 14.67; S, 11.52.

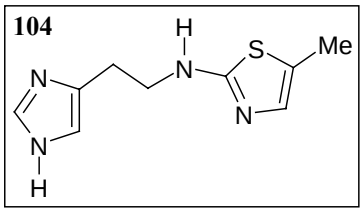
4.4.6 Reaction of Allenyl ITC 4a with Histamine and Histamine Derivatives

4.4.6.1 Synthesis of [2-(1*H*-Imidazol-4-yl)-ethyl]-(5-methyl-thiazol-2-yl)-amine 104

1-Isothiocyanato-propa-1,2-diene (**4a**) 10% in dry DMF (0.26 g, 2.70 mmol) was added dropwise to 2-(1*H*-imidazol-4-yl)-ethylamine **103** (0.30 g, 2.70 mmol) in 10 ml of DMF. After stirring 30 min at room temperature, the solvent was removed in vacuo, and the crude compound was isolated by flash chromatography from methanol and ethyl acetate (4:6) to give **[2-(1*H*-imidazol-4-yl)-ethyl]-(5-methyl-thiazol-2-yl)-amine 104** as white solid (0.35 g, 1.68 mmol, 62%). Recrystallization was done from methanol and ethyl acetate.

M.p. = 156–157 °C.

IR (KBr): 3447 (NH), 3218 (NH), 1591, 1451, 1135 cm^{-1}.



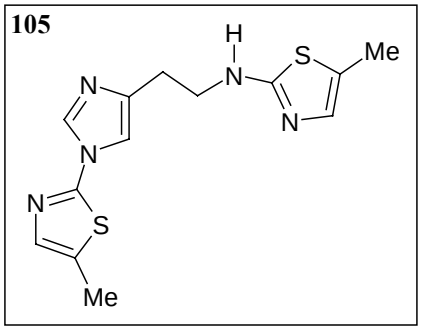
^{1}H NMR (CD_3OD): δ = 2.20 (d, ^4J = 1.5 Hz, 3H, Me), 2.86 (t, J = 7.2 Hz, 2H, CH_2), 3.47 (t, J = 7.2 Hz, 2H, NCH_2), 6.62 (q, ^4J = 1.5 Hz, 1H, =CH), 6.84 (dt, ^4J = 1.2 Hz, ^4J = 0.9 Hz, 1H, =CH), 7.57 (d, ^4J = 1.2 Hz, 1H, =CH).

^{13}C NMR (CD_3OD): δ = 2.26 (q, Me), 18.06 (t, C-2), 36.15 (t, C-1), 108.69 (d), 111.85 (s), 125.81 (d), 126.19 (s), 126.43 (d), 161.14 (s).

Anal. Calcd for $C_9H_{12}N_4S$ (208.15): C, 51.90; H, 5.81; N, 26.90; S, 15.40. **Found:** C, 51.51; H, 5.98; N, 26.73; S, 15.86.

4.4.6.2 Synthesis of (5-Methyl-thiazol-2-yl)-{2-[1-(5-methyl-thiazol-2-yl)-1*H*-imidazol-4-yl]-ethyl}-amine 105

1-Isothiocyanato-propa-1,2-diene (**4a**) 10% in dry DMF (0.140 g, 1.44 mmol) was added dropwise to [2-(1*H*-imidazol-4-yl)-ethyl]-(5-methyl-thiazol-2-yl)-amine **104** (0.30 g, 1.44 mmol) in 10 ml of DMF. After 30 minutes stirring at room temperature, the solvent was removed in vacuo, and the crude compound was separated by flash chromatography using THF and *n*-hexane (2:8) to afford **(5-methyl-thiazol-2-yl)-{2-[1-(5-methyl-thiazol-2-yl)-1*H*-imidazol-4-yl]-ethyl}-amine 105** as white solid (0.37 g, 1.21 mmol, 84%). Recrystallization was done from diethyl ether.



M.p. = 115−116 °C.

IR (KBr): 3195 (NH), 2923, 1572, 1474, 1144 cm^{-1}.

^{1}H NMR (CD_3OD): δ = 2.23 (d, ^4J = 1.2 Hz, 3H, Me), 2.47 (d, ^4J = 1.2 Hz, 3H, Me), 2.88 (t, J = 6.9 Hz, 2H, CH_2), 3.53 (t, J = 6.9 Hz, 2H, NCH_2), 6.63 (q, ^4J = 1.2 Hz, 1H, =CH), 7.28 (q, ^4J = 1.2 Hz, 1H, =CH), 7.46 (dt, ^4J = 1.4 Hz, ^4J = 0.9 Hz, 1H, =CH), 8.22 (d, ^4J = 1.4 Hz, 1H, =CH).

^{1}H NMR ($CDCl_3$): δ = 2.25 (d, ^4J = 1.5 Hz, 3H, Me), 2.45 (d, ^4J = 1.2 Hz, 3H, Me), 2.91 (t, J = 6.6 Hz, 2H, CH_2), 3.57 (t, J = 6.6 Hz, 2H, NCH_2), 5.71 (br, 1H, NH), 6.70 (q, ^4J = 1.5 Hz, 1H, =CH), 7.18 (q, ^4J = 1.2 Hz, 1H, =CH), 7.22 (dt, ^4J = 1.5 Hz, ^4J = 0.9 Hz, 1H, =CH), 8.02 (d, ^4J = 1.5 Hz, 1H, =CH).

^{13}C NMR ($CDCl_3$): δ = 11.91 (q, Me), 11.93 (q, Me), 27.55 (t, C-2), 44.84 (t, C-1), 114.52 (d), 120.79 (s), 130.57 (s), 134.84 (d), 135.34 (d), 137.51 (d), 141.30 (s), 155.26 (s), 168.67 (s).

Anal. Calcd for $C_{13}H_{15}N_5S_2$ (305.43): C, 51.12; H, 4.95; N, 22.93; S, 21.00. **Found:** C, 50.52; H, 5.00; N, 23.04; S, 20.70.

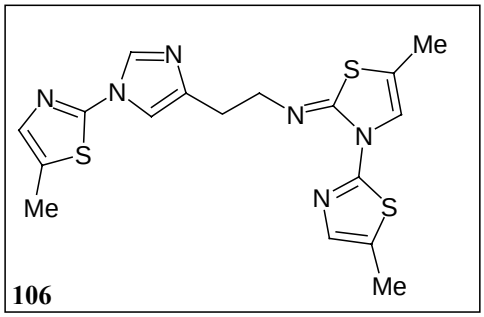
4.4.6.3 Synthesis of *Z*-*N*-(5,5'-Dimethyl-2,3'-bi-thiazol-2'-ylidene)-{2-[1-(5-methyl-thiazol-2-yl)-1*H*-imidazol-4-yl]-ethyl}-amine 106

Method **A**

1-Isothiocyanato-propa-1,2-diene (**4a**) 10% in dry THF (0.16 g, 1.64 mmol) was added dropwise to (5-methyl-thiazol-2-yl)-{2-[1-(5-methyl-thiazol-2-yl)-1*H*-imidazol-4-yl]-ethyl}-amine **105** (0.50 g, 1.64 mmol) in 10 ml of dry THF. After stirring 2 h at room temperature, the solvent was removed in vacuo, and the crude compound was separated by flash chromatography using acetone and *n*-hexane (1:1) to yield ***Z*-*N*-(5,5'-dimethyl-2,3'-bi-thiazol-2'-ylidene)-{2-[1-(5-methyl-thiazol-2-yl)-1*H*-imidazol-4-yl]-ethyl}-amine 106** as white solid (0.53 g, 1.31 mmol, 80%). Recrystallization was carried out from acetone and *n*-hexane.

Method **B**

1-Isothiocyanato-propa-1,2-diene (**4a**) 10% in dry DMF (1.05 g, 10.8 mmol) was added dropwise to 2-(1*H*-imidazol-4-yl)-ethylamine **103** (0.30 g, 2.70 mmol) in 5 ml of dry DMF. After 3 h stirring at room temperature, the solvent was removed in vacuo and the crude compound was separated by flash chromatography from acetone and *n*-hexane (1:1) to furnish ***Z*-*N*-(5,5'-dimethyl-2,3'-bi-thiazol-2'-ylidene)-{2-[1-(5-methyl-thiazol-2-yl)-1*H*-imidazol-4-yl]-ethyl}-amine 106** as white solid (0.42 g, 2.02 mmol, 51%). Recrystallization was done from acetone and *n*-hexane.



106

M.p. = 137–142 °C

IR ($CDCl_3$): 2922, 1650, 1623, 1482, 1145 cm^{-1}.

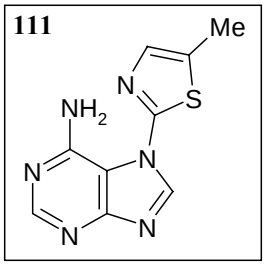
^{1}H NMR ($CDCl_3$): δ = 2.16 (d, ^4J = 1.2 Hz, 3H, Me), 2.34 (d, ^4J = 1.2 Hz, 3H, Me), 2.44 (d, ^4J = 1.2 Hz, 3H, Me), 3.05 (t, J = 7.1 Hz, 2H, CH_2), 3.54 (t, J = 7.2 Hz, 2H, NCH_2), 7.06 (q, ^4J = 1.5 Hz, 1H, =CH), 7.17 (d, ^4J = 1.2 Hz, 1H, imidazole-H), 7.34 (q, ^4J = 1.5 Hz, 1H, =CH), 7.40 (q, ^4J = 1.5 Hz, 1H, =CH), 8.05 (d, ^4J = 1.2 Hz, 1H, imidazole-H).

^{13}C-NMR ($CDCl_3$): δ = 11.46 (q, Me), 11.97 (q, Me), 13.76 (q, Me), 29.79 (t, C-2), 53.99 (t, C-1), 113.62 (s), 114.66 (d), 119.17 (d), 127.39 (s), 130.19 (s), 134.10 (d), 134.38 (d), 137.50 (d), 142.71 (s), 152.99 (s), 155.19 (s), 155.67 (s).

Anal. Calcd for $C_{17}H_{18}N_6S_3$ (402.57): C, 50.72; H, 4.51; N, 20.88; S, 23.90. **Found:** C, 50.82; H, 4.62; N, 20.22; S, 23.43.

4.4.7 Synthesis of 7-(5-Methyl-thiazol-2-yl)-7*H*-purin-6-ylamine 111

1-Isothiocyanato-propa-1,2-diene (**4a**) 10% in dry DMF (2.51 g, 25.90 mmol) was added dropwise to 9*H*-purin-6-ylamine (adenine) **107** (0.50 g, 3.70 mmol) in 10 ml of dry DMF. After four days stirring at room temperature, the solvent was removed in vacuo, and the crude compound was extracted using hot methanol to give **7-(5-methyl-thiazol-2-yl)-7*H*-purin-6-ylamine 111** as beige solid (0.36 g, 1.55 mmol, 42%). Recrystallization was done from methanol and ethyl acetate.



M.p. = 260–265 °C.

IR (KBr): 3254 (NH_2), 1650 (C=C), 1485 (C=N), 1145 (S–C) cm^{-1}.

^{1}H NMR (d_6-DMSO): δ = 2.45 (d, ^4J = 1.2 Hz, 3H, Me), 7.47 (q, ^4J = 1.2 Hz, 1H, =CH), 7.95 (br s, NH_2), 8.26 (s, 1H), 8.89 (s, 1H).

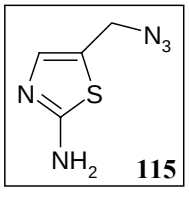
^{13}C NMR (d_6-DMSO): δ = 11.51 (q, Me), 109.47 (s), 131.67 (s), 136.72 (d), 144.92 (d), 151.92 (s), 153.93 (d), 156.02 (s), 160.05 (s).

Anal. Calcd for $C_9H_8N_6S$ (232.27): C, 46.55; H, 3.45; N, 36.21; S, 13.79. **Found:** C, 46.38; H, 3.60; N, 35.76; S, 13.70.

4.5 Advanced Succeeding Reactions of ITC 4a: Synthesis of Bifunctional Thiazoles

4.5.1 Reaction of Allenyl ITC 4a with Hydrazoic Acid

A solution of hydrazoic acid was prepared by addition of concentrated H_2SO_4 (96%, 4.93 g, 2.8 ml, 50.3 mmol) to a solution of sodium azide (6.50 g, 100 mmol) in 20 ml H_2O and 40 ml $CHCl_3$.[83] The organic layer was dried ($MgSO_4$) and stirred, after addition of 1-isothiocyanato-propa-1,2-diene (**4a**) 10% in $CHCl_3$ (0.200 g, 2.06 mmol), for three days in a dark and closed system at room temperature. The excess amount of hydrazoic acid was removed under vacuum in the fume hood. The reaction mixture was concentrated and purified by flash column chromatography using *n*-hexane and THF (6:4). The obtained product was recrystallized from CH_2Cl_2 and *n*-hexane to afford **5-azidomethyl-thiazol-2-ylamine 115** as yellow needles (0.19 g, 1.23 mmol, 60%).



M.p. = 87–88 °C.

IR (neat): 3410 (NH_2), 2101 (N_3), 1619, 1517 cm^{-1}.

^{1}H NMR (C_6D_6): δ = 3.49 (br s, 2H, CH_2N_3), 3.77 (br s, 2H, NH_2), 6.68 (t, ^4J = 0.9 Hz, 1H, H-4).

^{1}H NMR ($CDCl_3$): δ = 4.33 (s, 2H, CH_2N_3), 5.00 (br s, 2H, NH_2), 7.01 (s, 1H, H-4).

^{13}C NMR ($CDCl_3$): δ = 47.18 (t, CH_2N_3), 121.04 (s, C-5), 138.63 (d, C-4), 169.28 (s, C-2).

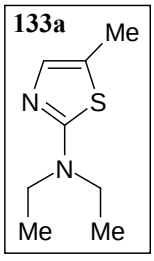
Anal. Calcd for $C_4H_5N_5S$ (155.20): C, 30.96; H, 3.25; N, 45.13. **Found:** C, 31.15; H, 3.48; N, 44.99.

4.5.2 Reaction of Allenyl ITC 4a with *N,N*-Disubstituted Hydroxylamine Derivatives

4.5.2.1 Reaction of Allenyl ITC 4a with *N,N*-Diethylhydroxylamine 130a

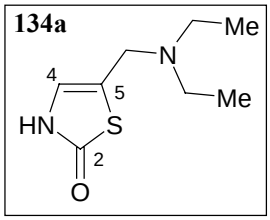
1-Isothiocyanato-propa-1,2-diene (**4a**) (10% in dry THF, 0.33 g, 3.37 mmol) was added dropwise under nitrogen to *N,N*-diethylhydroxylamine **130a** (0.20 g, 2.25 mmol) in 10 ml of dry THF at –5 °C. After 1 h at –5 °C, the reaction mixture was stirred overnight at room temperature. The solvent was removed under vacuum, and the crude compounds were separated by flash column chromatography using first diethyl ether and *n*-hexane (4:6) to give **diethyl-(5-methyl-thiazole-2-yl)-amine 133a**[86] as colorless oil (0.11 g, 0.65 mmol, 29%) followed then by elution with methanol and diethyl ether (7:93) to afford **5-diethylamino-methyl-3*H*-thiazol-2-one 134a** as white solid (0.21 g, 1.25 mmol, 55%); recrystallization was done from diethyl ether and *n*-hexane.

Data of **133a**[86]



IR (neat): 2971, 1539, 1120 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 1.19 (t, ^3J = 7.0 Hz, 6H, CH_2Me), 2.61 (d, ^4J = 1.2 Hz, 3H, Me-5), 3.41 (q, ^3J = 7.0 Hz, 4H, CH_2Me), 6.75 (q, ^4J = 1.2 Hz, 1H, H-4).
^{13}C-NMR ($CDCl_3$): δ = 11.84 (q, Me-5), 12.53 (q, CH_2Me), 45.04 (t, CH_2), 119.59 (s, C-5), 135.99 (d, C-4), 168.78 (s, C-2).
GC–MS; *m*/*z* (%): 170 [M^+] (27), 155 (18), 141 (41), 127 (100), 73 (32).

Data of **134a**



M.p. = 80–82 °C.
IR (CCl_4): 3148 (NH), 2972, 1659 (C=O), 1096 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 1.02 (t, ^3J = 7.2 Hz, 6H, CH_2Me), 2.55 (q, ^3J = 7.2 Hz, 4H, CH_2Me), 3.46 (d, ^4J = 1.2 Hz, 2H, CH_2 at C-5), 6.44 (t, ^4J = 1.2 Hz, 1H, H-4), 9.49 (br s, 1H, NH).
^{13}C NMR ($CDCl_3$): δ = 11.69 (q, CH_2Me), 46.29 (t, CH_2Me), 50.74 (t, CH_2 at C-5), 117.08 (s, C-5), 120.62 (d, C-4), 176.07 (s, C-2), assignments by C–H shift correlation.

^{15}N NMR ($CDCl_3$): δ = –315.75 (s, NEt_2), –214.64 (d, N-3).

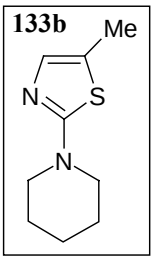
ESI–MS ($C_8H_{14}N_2OS$). **Calculated:** for $[M+H]^+$ 187.0900. **Found:** 187.0903.

Anal. Calcd for $C_8H_{14}N_2OS$ (186.28): C, 51.58; H, 7.58; N, 15.04; S, 17.21. **Found:** C, 51.61; H, 7.35; N, 14.94; S, 16.90.

4.5.2.2 Reaction of Allenyl ITC 4a with *N*-Hydroxypiperidine 130b

1-Isothiocyanato-propa-1,2-diene (**4a**) (10% in dry THF, 0.19 g, 1.96 mmol) was added dropwise under nitrogen at –5 °C to piperidinol **130b** (0.10 g, 0.99 mmol) in 10 ml of dry THF. After 1 h at –5 °C, the reaction mixture was stirred 20 h at room temperature. The solvent was removed under vacuum and the crude compounds were separated by flash column chromatography using first diethyl ether and *n*-hexane (4:6) to yield **2-(piperidin-1-yl)-5-methyl-thiazole 133b** as colorless oil (0.054 g, 0.296 mmol, 30%) followed then by elution with methanol and diethyl ether (7:93) to furnish **5-piperidin-1-ylmethyl-3*H*-thiazol-2-one 134b** as white solid (0.078 g, 0.39 mmol, 40%); recrystallization was done from diethyl ether and *n*-hexane.

Data of **133b**



IR (CCl_4): 2942, 1516, 1122 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.61–1.67 (m, 6H, H-3', H-4', H-5'), 2.27 (d, ^4J = 1.2 Hz, 3H, Me-5), 3.38 (m, 4H, H-2', H-6'), 6.78 (q, ^4J = 1.2 Hz, 1H, H-4).

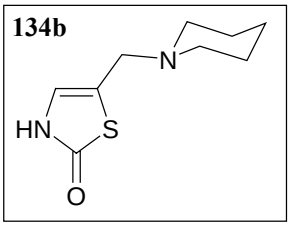
^{13}C NMR ($CDCl_3$): δ = 11.87 (q, Me-5), 24.08 (t, C-4'), 24.94 (t, C-3', C-5'), 49.42 (t, C-2', C-6'), 121.01 (s, C-5), 135.88 (d, C-4), 171.02 (s, C-2).

GC–MS; *m*/*z* (%): 182 [M^+] (52), 153 (56), 126 (64), 99 (40), 72 (52), 41 (100).

ESI–MS ($C_9H_{14}N_2S$). **Calculated:** for $[M+H]^+$ 183.0950. **Found:** 183.0997.

Anal. Calcd for $C_9H_{14}N_2S$ (182.29): C, 59.30; H, 7.74; N, 15.37. **Found**: C, 59.59; H, 7.16; N, 15.48.

Data of **134b**



M.p. = 136–138 °C.

IR (CCl_4): 3138 (NH), 2936, 1659 (C=O), 1097 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.41 (m, 2H, H-4"), 1.56 (m, 4H, H-3" and H-5"), 2.38 (m, 4H, H-2" and H-6"), 3.33 (d, ^4J = 0.9 Hz, 2H, H-1'), 6.44 (t, ^4J = 0.9 Hz, 1H, H-4), 9.87 (br s, 1H, NH).

^{13}C NMR ($CDCl_3$): δ = 24.01 (t, C-4"), 25.58 (t, C-3", C-5"), 53.78 (t, C-2", C-6"), 56.43 (t, C-1'), 118.10 (d, C-4), 118.85 (s, C-5), 176.27 (s, C-2).

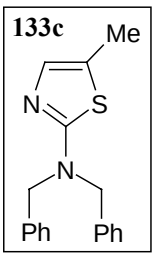
ESI–MS ($C_8H_{14}N_2OS$). $[M+H]^+$ 199.08

Anal. Calcd for $C_9H_{14}N_2OS$ (198.29): C, 54.52; H, 7.12; N, 14.13; S, 16.17. **Found:** C, 54.45; H, 6.83; N, 13.91; S, 16.81.

4.5.2.3 Reaction of Allenyl ITC 4a with *N,N*-Dibenzylhydroxylamine 130c

1-Isothiocyanato-propa-1,2-diene (**4a**) (10% in dry THF, 0.14 g, 1.44 mmol) was added dropwise under nitrogen to *N,N*-dibenzylhydroxylamine **130c** (0.20 g, 0.94 mmol) in 10 ml of dry THF at –5 °C. After 1 h at –5 °C, the reaction mixture was stirred 21 h at room temperature. The solvent was removed under vacuum, and the crude compounds were separated by flash column chromatography using first diethyl ether and *n*-hexane (3:7) to give **2-dibenzylamino-5-methyl-thiazole 133c** as colorless oil (0.091 g, 0.31 mmol, 33%) followed then by eluting with ethyl acetate and *n*-hexane (6:4) to afford **5-[(dibenzylamino)-methyl]-3*H*-thiazol-2-one 134c** as white solid (0.10 g, 0.32 mmol, 35%); recrystallization was done from diethyl ether and *n*-hexane.

Data of **133c**



IR (CCl_4): 3063, 2920, 1533, 1212 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.31 (d, ^4J = 1.2 Hz, 3H, Me-5), 4.64 (s, 4H, H-1'), 6.86 (q, ^4J = 1.2 Hz, 1H, H-4), 7.25–7.37 (m, 10H, 2×Ph).

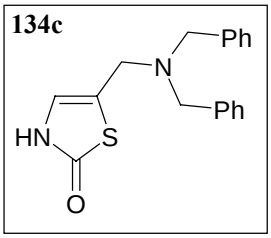
^{13}C NMR ($CDCl_3$): δ = 11.95 (q, Me-5), 53.34 (t, C-1'), 120.85 (s, C-5), 127.37

(d, 2×Ph$_p$), 127.60 (d, 4×Ph), 128.56 (d, 4×Ph), 136.10 (d, C-4), 136.79 (s, 2×Ph$_i$), 170.30 (s, C-2).

GC–MS; *m*/*z* (%): 294 [M$^+$] (2), 203 (26), 91 (100), 65 (35).

Anal. Calcd for $C_{18}H_{18}N_2S$ (294.42): C, 73.34; H, 6.16; N, 9.51; S, 10.89. **Found:** C, 73.11; H, 5.96; N, 9.36; S, 11.07.

Data of **134c**



M.p. = 169–170 °C.

IR (CCl_4): 3171 (NH), 1658 (C=O), 1493, 1120, 1097 cm^{-1}.

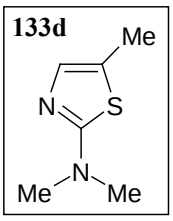
^{1}H NMR ($CDCl_3$): δ = 3.43 (s, 2H, H-1'), 3.59 (s, 4H, 2×C*H*$_2$Ph), 6.45 (s, 1H, H-4), 7.24–7.41 (m, 10H, 2×Ph), 9.74 (br s, 1H, NH).

^{13}C NMR ($CDCl_3$): δ = 50.99 (t, C-1'), 57.34 (t, 2×*C*H$_2$Ph), 117.45 (d, C-4), 120.41 (s, C-5), 127.14 (d, 2×Ph$_p$), 128.34 (d, 4×Ph), 128.70 (d, 4×Ph), 138.65 (s, 2×Ph$_i$), 175.94 (s, C-2).

ESI–MS ($C_{18}H_{18}N_2OS$). **Calculated:** for [M+H]$^+$ 311.1246. **Found:** 311.1213.

4.5.2.4 Reaction of Allenyl ITC 4a with *N,N*-Dimethylhydroxylamine Hydrochloride 130d

1-Isothiocyanato-propa-1,2-diene (**4a**) (10% in THF, 0.30 g, 3.09 mmol) was added dropwise to a stirred mixture of 20 ml of THF/H_2O = 1:1 solution containing *N,N*-dimethylhydroxylamine hydrochloride **130d** (0.15 g, 1.54 mmol) and sodium bicarbonate (0.11 g, 1.53 mmol) at 0 °C. After 1 h the ice bath was removed, and stirring was continued for 17 h at room temperature. Diethyl ether (30 ml) was added, and the organic layer was separated. The aqueous layer was extracted with diethyl ether (3×10 ml). The organic extracts were combined, dried ($MgSO_4$), concentrated by vacuum evaporation, and the crude compound was separated by flash chromatography using diethyl ether and *n*-hexane (4:6) to give **2-dimethylamino-5-methyl-thiazole 133d**[90] as colorless oil (0.103 g, 0.746 mmol, 49%).



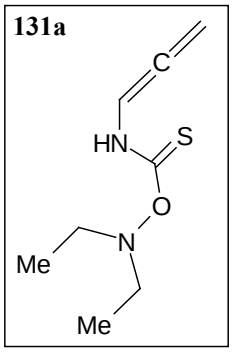
^{1}H NMR ($CDCl_3$): δ = 2.23 (d, ^4J = 1.2 Hz, 3H, Me-5), 2.98 (s, 6H, NMe_2), 6.75 (q, ^4J = 1.2 Hz, 1H, H-4).

^{13}C NMR ($CDCl_3$): δ = 11.85 (q, Me-5), 40.03 (q, NMe_2), 120.93 (s, C-5), 136.26 (d, C-4), 170.38 (s, C-2).

GC–MS; *m*/*z* (%): 142 [M^+] (47), 113 (89), 100 (30), 71 (54), 44 (100).

4.5.2.5 Detection of Compounds 132a–c and 134a–c in NMR Experiments

Hydroxylamines **130a** (0.028 g, 0.31 mmol), **130b** (0.031 g, 0.31 mmol), and **130c** (0.066 g, 0.31 mmol) were added to 1-isothiocyanato-propa-1,2-diene (**4a**) (10% in dry $CDCl_3$, 0.015 g, 0.0155 mmol) at –5 °C. After 13, 15, and 17 min, respectively, ^{1}H NMR and IR showed no remaining allene **4a**. The percentage yields were measured using grease as a standard and founds to be 86, 83, and 80% for **131a**, **131b**, **131c**, respectively. After 18, 20, and 21 h, respectively at room temperature the reactions were completed to yield one major product in each case, i.e. the thiazoles **134a–c** with yields of 60, 51, and 61%, respectively (grease was also used as a standard). After 13–17 min as well as after 18–21 h, no signals of **133** could be observed.



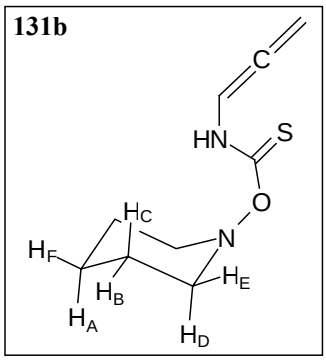
Data of **Propa-1,2-dienyl-thiocarbamic Acid *O*-Diethylamino Ester 131a**

IR ($CDCl_3$): 1964 (wk, allene) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.08 (t, ^3J = 7.2 Hz, 6H, 2×CH_3), 2.95 (q, ^3J = 7.2 Hz, 4H, 2×CH_2), 5.33 (d, ^4J = 6.6 Hz, 2H, =CH_2), 7.25 (t, ^4J = 6.6 Hz, 1H, =CH), 9.42 (br s, 1H, NH).

^{13}C NMR ($CDCl_3$): δ = 11.63 (q, 2×CH_3), 53.30 (t, 2×CH_2), 86.54 (t, =CH_2), 96.86 (d, =CH), 186.21 (s, C=S), 202.49 (s, =C=).

Data of **Propa-1,2-dienyl-thiocarbamic Acid *O*-Piperidin-1-yl Ester 131b**

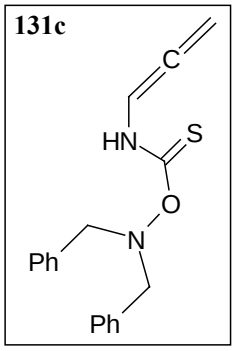


IR ($CDCl_3$): 1960 (wk, allene) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.22 (br qt, $^2J_{AF} \cong {}^3J_{AC} \cong 13.2$ Hz, $^3J_{AB} \cong 3$ Hz, 1H, H_A), 1.62 (qd, $J \cong 11.6$ Hz, $J \cong 3.8$ Hz, 3H, $H_F + 2\times H_C$), 1.83 (dm, $^2J_{BC} \cong 13$ Hz, 2H, $2\times H_B$), 2.80 (dt, $^2J_{DE} \cong {}^3J_{DC} \cong 11$ Hz, $^3J_{DB} \cong 3$ Hz, 2H, $2\times H_D$), 3.26 (br dt, $^2J_{ED} \cong 9.9$ Hz, $^3J_{EC} \cong {}^3J_{EB} \cong 3$ Hz, 2H, $2\times H_E$), 5.33 (d, ^4J = 6.6 Hz, 2H, $=CH_2$), 7.24 (t, ^4J = 6.6 Hz, 1H, =CH), 9.46 (br s, 1H, NH).

^{13}C NMR ($CDCl_3$): δ = 22.46 (t), 25.13 (t, $2\times CH_2$), 56.76 (t, $2\times CH_2$), 86.55 (t, $=CH_2$), 96.92 (d, =CH), 184.46 (s, C=S), 202.59 (s, =C=).

Data of **Propa-1,2-dienyl-thiocarbamic Acid *O*-Dibenzylamino Ester 131c**



IR ($CDCl_3$): 1957 (wk, allene) cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.13 (s, 4H, $2\times CH_2$), 5.24 (d, ^4J = 6.6 Hz, 2H, $=CH_2$), 6.84 (dt, ^3J = 9.9 Hz, ^4J = 6.6 Hz, 1H, =CH), 7.32 (m, 10H, 2×Ph), 8.72 (d, ^3J = 9.6 Hz, 1H, NH).

^{13}C NMR ($CDCl_3$): δ = 62.65 (t, $2\times CH_2$), 86.14 (t, $=CH_2$), 96.55 (d, =CH), 128.24 (d, $2\times Ph_p$), 128.61 (d, 4×Ph), 129.53 (d, 4×Ph), 134.31 (s, $2\times Ph_i$), 184.45 (s, C=S), 202.32 (s, =C=).

4.5.2.6 Control Experiment for the Formation of 2-(Piperidin-1-yl)-5-methyl-thiazole 133b and 2-Dibenzylamino-5-methyl-thiazole 133c

General Procedure

1-Isothiocyanato-propa-1,2-diene (**4a**) (0.20 g, 2.06 mmol) in 2 ml THF was added slowly at 0 °C to a solution of piperidine **140** (0.42 g, 4.93 mmol) or dibenzylamine **141** (0.36 g, 4.92 mmol) and toluene-4-sulfonic acid monohydrate (0.47 g, 2.47 mmol) in 4 ml THF and 2 ml water. After stirring three days at room temperature, water (10 ml) was added, and the product

was extracted with diethyl ether (3×10 ml). The organic layers were combined, dried ($MgSO_4$), and concentrated by vacuum evaporation. Purification of the crude products was carried out by using flash chromatography (diethyl ether and *n*-hexane 2:8 and 3:8, respectively) to afford **2-(piperidin-1-yl)-5-methyl-thiazole 133b** (0.16 g, 0.88 mmol, 43%) as a colorless oil and **2-dibenzylamino-5-methyl-thiazole 133c** (0.50 g, 1.68 mmol, 82%) as a colorless oil.

The spectral data are mentioned in sections **4.5.2.2** and **4.5.2.3**, respectively.

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APPENDIX: The X-ray Data of the Measured Compounds

2-[1-(5-Methyl-thiazol-2-yl)-1*H*-pyrazol-3-yl]-pyridine 97c ($C_{12}H_{10}N_4S$)

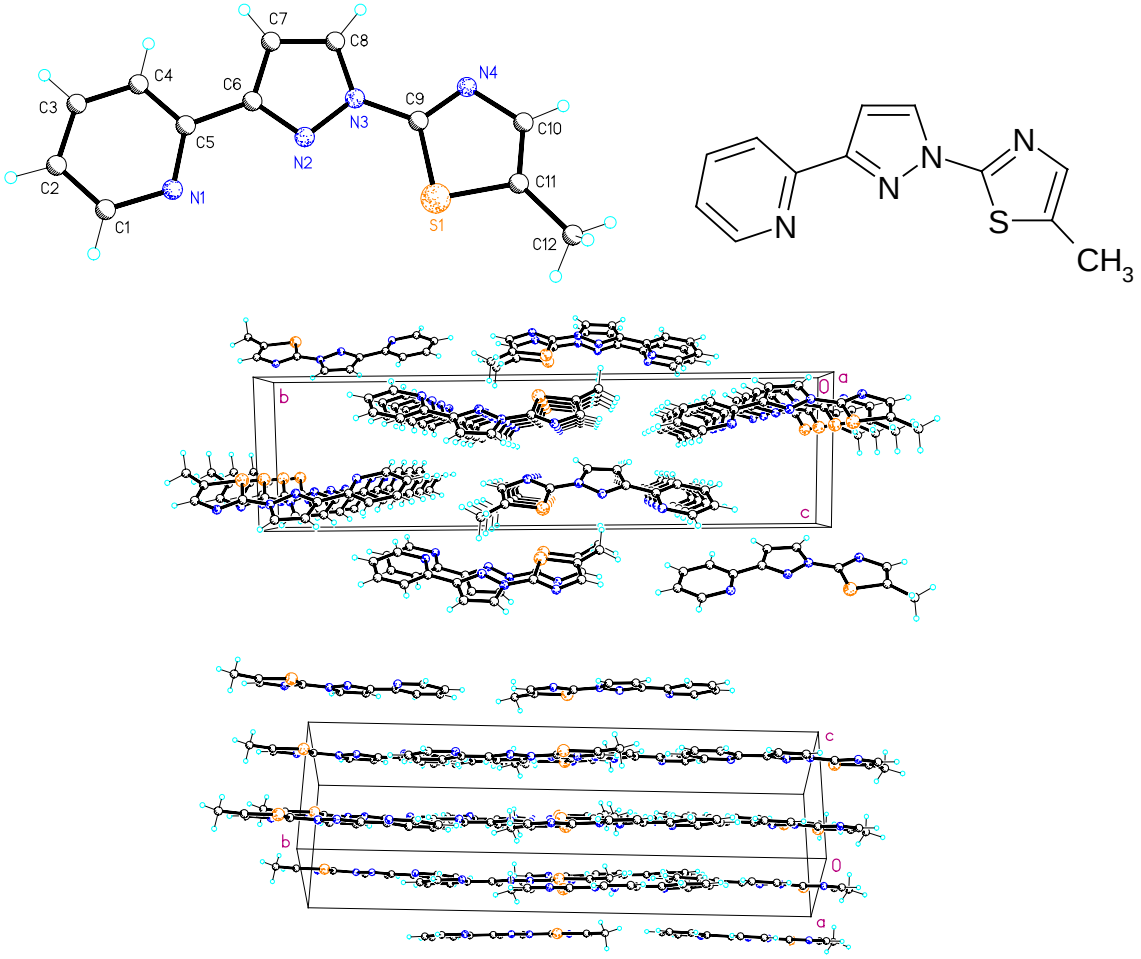


Table 1 Crystal data and structure refinement for 97c

Empirical formula	$C_{12}H_{10}N_4S$
Formula weight	242.30
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/c
Unit cell dimensions	a = 5.6627(10) Å b = 27.640(5) Å c = 7.5634(14) Å β= 99.976(3)°
Volume	1165.9(4) $Å^3$
Z	4
Density (calculated)	1.380 Mg/m^3
Absorption coefficient	0.259 mm^{-1}

F(000)	504
Crystal size	0.4 x 0.3 x 0.02 mm^3
Theta range for data collection	1.47 to 26.54°.
Index ranges	-7<=h<=6, 0<=k<=34, 0<=l<=9
Reflections collected	11238
Independent reflections	2464 [R(int) = 0.0424]
Completeness to theta = 26.54°	98.6 %
Absorption correction	Multiscan
Max. and min. transmission	0.99999 and 0.81252
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2389 / 0 / 156
Goodness-of-fit on F^2	1.061
Final R indices [I>2sigma(I)]	R1 = 0.0634, wR2 = 0.1632
R indices (all data)	R1 = 0.0976, wR2 = 0.1946
Extinction coefficient	0.0028(15)
Largest diff. peak and hole	0.490 and -0.404 e.$Å^{-3}$

Table 2 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 97c.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(5)	-317(6)	3130(1)	7554(5)	54(1)
C(6)	-1224(6)	3618(1)	7083(4)	49(1)
N(2)	108(5)	4010(1)	7573(4)	50(1)
N(3)	-1335(5)	4386(1)	6938(4)	50(1)
C(7)	-3504(6)	3752(1)	6140(5)	58(1)
C(8)	-3521(6)	4240(1)	6061(5)	56(1)
C(9)	-490(6)	4858(1)	7226(4)	48(1)
N(4)	-1769(5)	5232(1)	6661(4)	61(1)
S(1)	2334(2)	4966(1)	8397(1)	56(1)
C(10)	-435(7)	5643(1)	7193(5)	64(1)
C(11)	1797(6)	5579(1)	8128(5)	54(1)
C(12)	3635(7)	5949(1)	8856(6)	67(1)
N(1)	2009(6)	3050(1)	8448(5)	78(1)
C(4)	-1849(6)	2769(1)	7049(5)	57(1)
C(2)	1134(9)	2206(2)	8322(7)	81(1)
C(1)	2714(8)	2576(2)	8839(6)	74(1)
C(3)	-1111(9)	2323(2)	7431(7)	89(2)

Table 3 Bond lengths [Å] and angles [°] for 97c.

C(5)-C(4)	1.333(5)	C(6)-N(2)-N(3)	104.2(3)
C(5)-N(1)	1.390(5)	N(2)-N(3)-C(8)	112.8(3)
C(5)-C(6)	1.466(5)	N(2)-N(3)-C(9)	119.5(3)
C(6)-N(2)	1.334(4)	N(8)-N(3)-C(9)	127.7(3)
C(6)-C(7)	1.411(5)	C(8)-N(7)-C(6)	106.4(3)
N(2)-N(3)	1.357(4)	C(7)-C(8)-N(3)	106.0(3)
N(3)-C(8)	1.360(4)	N(4)-C(9)-N(3)	122.7(3)
N(3)-C(9)	1.395(4)	N(4)-C(9)-S(1)	116.8(3)
C(7)-C(8)	1.351(6)	N(3)-C(9)-S(1)	120.5(2)
C(9)-N(4)	1.291(4)	C(9)-N(4)-C(10)	108.3(3)
C(9)-S(1)	1.714(3)	C(9)-S(1)-C(11)	88.89(16)
N(4)-C(10)	1.385(5)	C(11)-C(10)-N(4)	117.3(3)
S(1)-C(11)	1.726(3)	C(10)-C(11)-C(12)	129.2(3)
C(10)-C(11)	1.349(5)	C(10)-C(11)-S(1)	108.7(3)

C(11)-C(12)	1.495(5)	C(12)-C(11)-S(1)	122.1(3)
N(1)-C(1)	1.387(5)	C(1)-N(1)-C(5)	117.9(4)
C(4)-C(3)	1.318(6)	C(3)-C(4)-C(5)	118.1(4)
C(2)-C(1)	1.370(6)	C(1)-C(2)-C(3)	117.9(4)
C(2)-C(3)	1.370(6)	C(2)-C(1)-N(1)	119.7(4)
C(4)-C(5)-N(1)	122.3(3)	C(4)-C(3)-C(2)	124.1(4)
C(4)-C(5)-C(6)	115.8(3)	N(2)-C(6)-C(7)	110.6(3)
N(1)-C(5)-C(6)	121.8(3)	N(2)-C(6)-C(5)	121.4(3)
C(7)-C(6)-C(5)	127.9(3)		

Table 4 Anisotropic displacement parameters ($Å^2 x\ 10^3$)for 97c. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

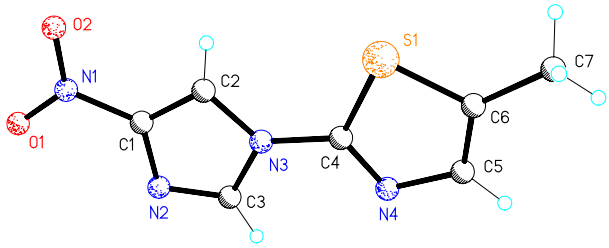
Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(5)	53(2)	55(2)	51(2)	-1(2)	4(2)	1(2)
C(6)	45(2)	52(2)	50(2)	-2(2)	3(1)	-4(1)
N(2)	44(2)	48(2)	55(2)	0(1)	0(1)	4(1)
N(3)	45(2)	53(2)	51(2)	-1(1)	0(1)	4(1)
C(7)	46(2)	64(2)	59(2)	1(2)	-2(2)	-2(2)
C(8)	41(2)	65(2)	56(2)	5(2)	-5(2)	4(2)
C(9)	45(2)	54(2)	44(2)	2(1)	1(1)	7(1)
N(4)	53(2)	55(2)	71(2)	8(2)	-1(2)	8(1)
S(1)	49(1)	49(1)	65(1)	-2(1)	-7(1)	6(1)
C(10)	62(2)	47(2)	80(3)	10(2)	5(2)	9(2)
C(11)	55(2)	47(2)	59(2)	0(2)	8(2)	4(2)
C(12)	69(2)	55(2)	74(3)	-4(2)	5(2)	-2(2)
N(1)	68(2)	76(2)	83(2)	0(2)	-1(2)	8(2)
C(4)	43(2)	44(2)	77(2)	1(2)	-7(2)	-5(1)
C(2)	88(3)	54(2)	97(3)	9(2)	4(3)	8(2)
C(1)	69(3)	64(3)	84(3)	8(2)	-4(2)	15(2)
C(3)	80(3)	61(3)	119(4)	0(3)	-2(3)	-14(2)

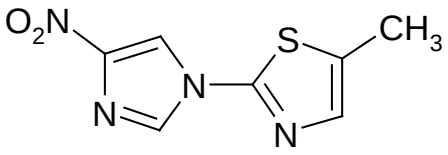
Table 5 Torsion angles [°] for 97c.

C(4)-C(5)-C(6)-N(2)	177.5(3)
N(1)-C(5)-C(6)-N(2)	-3.4(5)
C(4)-C(5)-C(6)-C(7)	-1.0(6)
N(1)-C(5)-C(6)-C(7)	178.1(4)
C(7)-C(6)-N(2)-N(3)	0.0(4)
C(5)-C(6)-N(2)-N(3)	-178.7(3)
C(6)-N(2)-N(3)-C(8)	-0.3(4)
C(6)-N(2)-N(3)-C(9)	179.8(3)
N(2)-C(6)-C(7)-C(8)	0.3(4)
C(5)-C(6)-C(7)-C(8)	178.9(3)
C(6)-C(7)-C(8)-N(3)	-0.4(4)
N(2)-N(3)-C(8)-C(7)	0.5(4)
C(9)-N(3)-C(8)-C(7)	-179.6(3)
N(2)-N(3)-C(9)-N(4)	-179.9(3)
C(8)-N(3)-C(9)-N(4)	0.2(6)
N(2)-N(3)-C(9)-S(1)	-0.9(4)
C(8)-N(3)-C(9)-S(1)	179.3(3)
N(3)-C(9)-N(4)-C(10)	178.8(3)
S(1)-C(9)-N(4)-C(10)	-0.3(4)
N(4)-C(9)-S(1)-C(11)	0.1(3)
N(3)-C(9)-S(1)-C(11)	-179.0(3)
C(9)-N(4)-C(10)-C(11)	0.3(5)

N(4)-C(10)-C(11)-C(12)	179.4(4)
N(4)-C(10)-C(11)-S(1)	-0.2(5)
C(9)-S(1)-C(11)-C(10)	0.1(3)
C(9)-S(1)-C(11)-C(12)	-179.6(3)
C(4)-C(5)-N(1)-C(1)	-0.9(6)
C(6)-C(5)-N(1)-C(1)	-180.0(3)
N(1)-C(5)-C(4)-C(3)	0.4(6)
C(6)-C(5)-C(4)-C(3)	179.5(4)
C(3)-C(2)-C(1)-N(1)	-0.2(7)
C(5)-N(1)-C(1)-C(2)	0.8(6)
C(5)-C(4)-C(3)-C(2)	0.3(8)
C(1)-C(2)-C(3)-C(4)	-0.4(8)

5-Methyl-2-(4-nitro-imidazol-1-yl)-thiazole 97h ($C_7H_6N_4O_2S$)





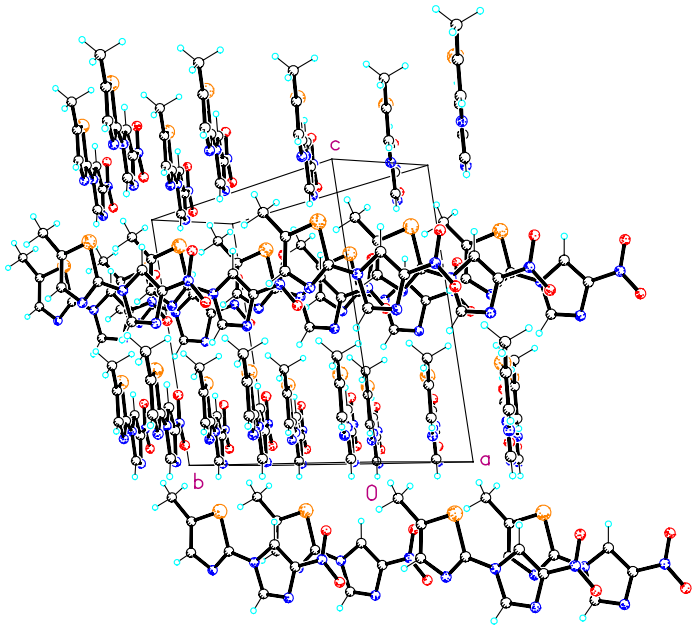


Table 1 Crystal data and structure refinement for 97h

Empirical formula	$C_7H_6N_4O_2S$
Formula weight	210.22
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	Cc

Unit cell dimensions	a = 3.942(3) Å b = 19.781(13) Å c = 11.283(8) Å β= 99.372(7)°.
Volume	868.0(10) $Å^3$
Z	4
Density (calculated)	1.609 Mg/m^3
Absorption coefficient	0.350 mm^{-1}
F(000)	432
Crystal size	0.4 x 0.3 x 0.2 mm^3
Theta range for data collection	2.06 to 26.64°.
Index ranges	-4<=h<=4, 0<=k<=24, -14<=l<=14
Reflections collected	4684
Independent reflections	1828 [R(int) = 0.0467]
Completeness to theta = 26.64°	99.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.99999 and 0.49273
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1777 / 2 / 128
Goodness-of-fit on F^2	1.089
Final R indices [I>2sigma(I)]	R1 = 0.0619, wR2 = 0.1530
R indices (all data)	R1 = 0.0668, wR2 = 0.1578
Absolute structure parameter	-0.01(14)
Largest diff. peak and hole	0.522 and -0.377 $e.Å^{-3}$

Table 2 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 97h.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
N(1)	11846(10)	4124(2)	6512(4)	51(1)
O(1)	12692(11)	3785(2)	5708(4)	74(1)
O(2)	12467(14)	3969(2)	7565(4)	81(1)
C(1)	10062(9)	4742(2)	6217(4)	40(1)
N(2)	9237(10)	4963(2)	5071(3)	49(1)
N(3)	7468(8)	5675(2)	6340(3)	37(1)
C(2)	9005(10)	5164(2)	7023(4)	39(1)
C(3)	7677(12)	5530(2)	5180(4)	49(1)
C(4)	5952(10)	6263(2)	6728(3)	37(1)
N(4)	4615(10)	6708(2)	6001(3)	49(1)
S(1)	5881(2)	6405(1)	8225(1)	45(1)
C(5)	3429(12)	7228(2)	6637(4)	51(1)
C(6)	3901(9)	7161(2)	7830(4)	41(1)
C(7)	2958(12)	7637(2)	8744(4)	53(1)

Table 3 Bond lengths [Å] and angles [°] for 97h.

N(1)-O(2)	1.213(6)	C(6)-C(5)-N(4)	116.5(4)
N(1)-O(1)	1.217(5)	C(5)-C(6)-C(7)	128.7(4)
N(1)-C(1)	1.423(6)	O(2)-N(1)-O(1)	123.8(4)
C(1)-C(2)	1.349(6)	O(2)-N(1)-C(1)	117.3(4)
C(1)-N(2)	1.354(6)	O(1)-N(1)-C(1)	118.9(4)
C(4)-S(1)	1.717(4)	C(2)-C(1)-N(2)	113.0(4)
N(4)-C(5)	1.379(6)	C(2)-C(1)-N(1)	124.7(4)
S(1)-C(6)	1.712(4)	N(2)-C(1)-N(1)	122.2(3)
C(5)-C(6)	1.335(7)	C(3)-N(2)-C(1)	103.4(4)
C(6)-C(7)	1.488(6)	N(4)-C(4)-S(1)	117.1(3)

N(2)-C(3)	1.294(6)	C(5)-C(6)-S(1)	109.4(3)
N(3)-C(2)	1.352(5)	C(7)-C(6)-S(1)	121.9(3)
N(3)-C(3)	1.355(6)	C(2)-N(3)-C(3)	107.5(3)
N(3)-C(4)	1.410(5)	C(2)-N(3)-C(4)	127.8(3)
C(4)-N(4)	1.258(6)	C(3)-N(3)-C(4)	124.7(4)
N(3)-C(4)-S(1)	121.0(3)	C(1)-C(2)-N(3)	103.7(4)
C(4)-N(4)-C(5)	108.9(4)	N(2)-C(3)-N(3)	112.3(4)
C(6)-S(1)-C(4)	88.1(2)	N(4)-C(4)-N(3)	121.9(4)

Table 4 Anisotropic displacement parameters ($Å^2$x 10^3)for 97h. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1)	45(2)	51(2)	57(2)	-6(2)	10(2)	3(2)
O(1)	82(3)	69(2)	72(3)	-13(2)	23(2)	18(2)
O(2)	104(3)	71(3)	63(2)	7(2)	2(2)	32(2)
C(1)	32(2)	42(2)	46(2)	-1(2)	7(2)	-4(2)
N(2)	51(2)	53(2)	44(2)	-5(2)	11(2)	2(2)
N(3)	29(1)	44(2)	39(2)	-1(1)	6(1)	-4(1)
C(2)	35(2)	45(2)	37(2)	1(2)	8(1)	-1(2)
C(3)	49(2)	56(3)	42(2)	3(2)	6(2)	1(2)
C(4)	32(2)	45(2)	35(2)	-1(2)	8(1)	-5(2)
N(4)	58(2)	49(2)	40(2)	2(2)	5(2)	5(2)
S(1)	45(1)	51(1)	38(1)	1(1)	7(1)	9(1)
C(5)	51(2)	46(2)	54(2)	2(2)	3(2)	8(2)
C(6)	29(2)	44(2)	48(2)	0(2)	2(2)	3(1)
C(7)	46(2)	56(2)	56(3)	-8(2)	6(2)	8(2)

Table 5 Torsion angles [°] for 97h.

O(2)-N(1)-C(1)-C(2)	-0.4(6)
O(1)-N(1)-C(1)-C(2)	-179.6(4)
O(2)-N(1)-C(1)-N(2)	-180.0(5)
O(1)-N(1)-C(1)-N(2)	0.8(6)
C(2)-C(1)-N(2)-C(3)	0.4(5)
N(1)-C(1)-N(2)-C(3)	-179.9(4)
N(2)-C(1)-C(2)-N(3)	-0.4(5)
N(1)-C(1)-C(2)-N(3)	179.9(3)
C(3)-N(3)-C(2)-C(1)	0.3(4)
C(4)-N(3)-C(2)-C(1)	-178.7(3)
C(1)-N(2)-C(3)-N(3)	-0.2(5)
C(2)-N(3)-C(3)-N(2)	0.0(5)
C(4)-N(3)-C(3)-N(2)	179.0(4)
C(2)-N(3)-C(4)-N(4)	179.4(4)
C(3)-N(3)-C(4)-N(4)	0.6(6)
C(2)-N(3)-C(4)-S(1)	-0.1(5)
C(3)-N(3)-C(4)-S(1)	-179.0(3)
N(3)-C(4)-N(4)-C(5)	-178.5(4)
S(1)-C(4)-N(4)-C(5)	1.1(5)
N(4)-C(4)-S(1)-C(6)	-1.4(4)
N(3)-C(4)-S(1)-C(6)	178.2(3)
C(4)-N(4)-C(5)-C(6)	-0.1(6)
N(4)-C(5)-C(6)-C(7)	179.0(4)
N(4)-C(5)-C(6)-S(1)	-0.9(5)
C(4)-S(1)-C(6)-C(5)	1.2(3)
C(4)-S(1)-C(6)-C(7)	-178.7(4)

_N_-(5,5'-dimethyl-2,3'-bi-1,3-thiazol-2'-ylidene)-_N_-{2-[1-(5-methyl-1,3-thiazol-2-yl)-1_H_-imidazol-4-yl]-ethyl}-amine 106 ($C_{17}H_{18}N_6S_3$)

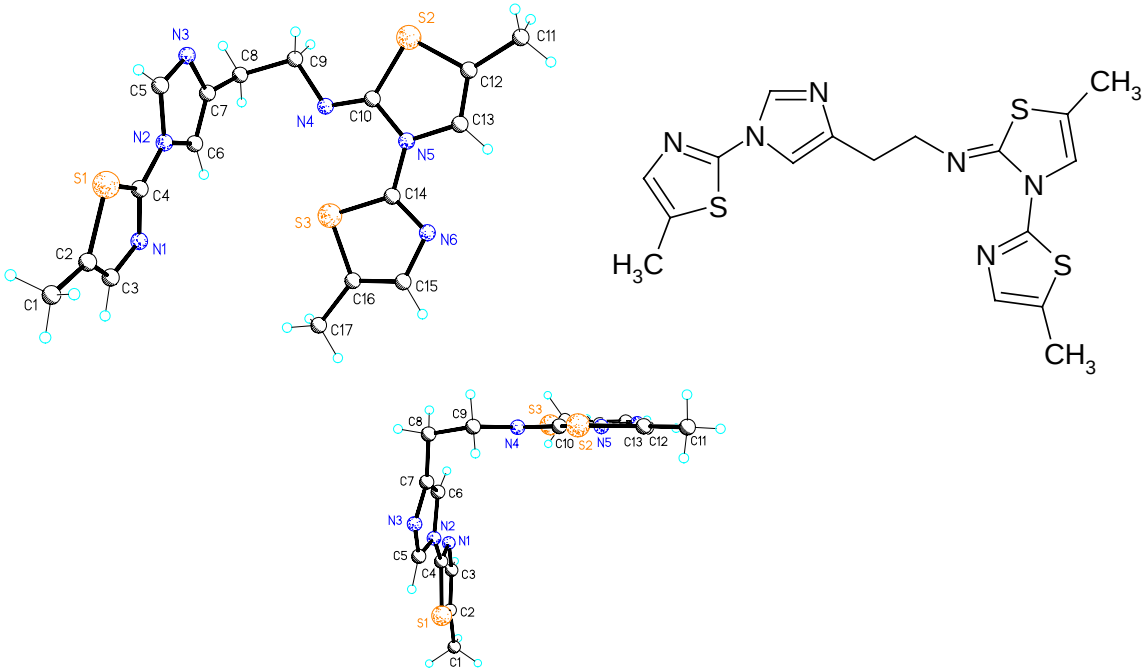


Table 1 Crystal data and structure refinement for 106.

Empirical formula	$C_{17}H_{18}N_6S_3$
Formula weight	402.55
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 6.0349(15) Å b = 8.321(2) Å c = 19.245(5) Å β = 91.218(5)°
Volume	945.6(4) $Å^3$
Z	2
Density (calculated)	1.414 Mg/m^3
Absorption coefficient	0.406 mm^{-1}
F(000)	420
Crystal size	0.4 x 0.05 x 0.05 mm^3
Theta range for data collection	2.15 to 26.45°.
Index ranges	-7<=h<=7, -10<=k<=10, -24<=l<=24
Reflections collected	9851
Independent reflections	8905 [R(int) = 0.0601]
Completeness to theta = 26.45°	94.4 %
Absorption correction	Empirical
Max. and min. transmission	0.99999 and 0.592434
Refinement method	Full-matrix least-squares on F^2

Data / restraints / parameters	8905 / 94 / 243
Goodness-of-fit on F^2	1.009
Final R indices [I>2sigma(I)]	R1 = 0.0873, wR2 = 0.2031
R indices (all data)	R1 = 0.1150, wR2 = 0.2208
Largest diff. peak and hole	0.670 and -0.602 e.Å^{-3}

Table 2 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for 106.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U (eq)
C(1)	3234(15)	5337(7)	-1211(3)	120(2)
C(2)	3910(10)	6506(5)	-578(2)	75(1)
C(3)	5834(9)	7119(7)	-269(3)	90(1)
N(1)	5889(6)	8123(4)	327(2)	60(1)
C(4)	3853(8)	8461(5)	504(2)	64(1)
S(1)	1870(2)	7410(2)	-48(1)	99(1)
N(2)	3401(7)	9561(4)	1102(2)	64(1)
C(6)	4872(8)	10366(5)	1639(2)	62(1)
C(7)	3722(8)	11291(5)	2083(2)	58(1)
N(3)	1501(7)	11124(5)	1848(2)	78(1)
C(5)	1372(9)	10118(6)	1262(2)	79(1)
C(8)	4490(9)	12303(5)	2773(2)	66(1)
C(9)	3741(9)	11560(4)	3399(2)	57(1)
N(4)	4839(6)	10063(3)	3421(1)	50(1)
C(10)	4216(6)	9210(4)	3872(2)	42(1)
C(11)	1173(8)	7146(5)	5394(2)	58(1)
C(12)	2551(7)	7684(4)	4824(2)	51(1)
S(2)	2143(2)	9482(1)	4501(1)	50(1)
C(13)	4118(7)	6957(5)	4471(2)	51(1)
N(5)	5109(5)	7780(3)	3950(2)	49(1)
C(14)	6915(7)	7226(4)	3562(2)	46(1)
N(6)	7674(6)	5936(4)	3685(2)	58(1)
S(3)	8102(2)	8190(1)	2911(1)	53(1)
C(15)	9415(8)	5668(5)	3246(2)	65(1)
C(16)	9894(7)	6702(5)	2801(2)	54(1)
C(17)	11691(9)	6721(6)	2279(2)	72(1)

Table 3 Bond distances [Å], bond angels [°] for 106.

C(1)-C(2)	1.447(6)	N(4)-C(9)-C(8)	109.2(3)
C(2)-C(3)	1.298(7)	C(10)-N(4)-C(9)	117.0(3)
C(2)-S(1)	1.779(5)	N(4)-C(10)-N(5)	122.8(3)
C(3)-N(1)	1.305(6)	N(4)-C(10)-S(2)	129.5(3)
N(1)-C(4)	1.334(6)	N(5)-C(10)-S(2)	107.7(2)
C(4)-N(2)	1.405(5)	C(13)-C(12)-C(11)	129.3(3)
C(4)-S(1)	1.647(5)	C(13)-C(12)-S(2)	110.2(3)
N(2)-C(6)	1.377(5)	C(11)-C(12)-S(2)	120.5(3)
N(2)-C(5)	1.386(6)	C(12)-S(2)-C(10)	92.59(17)
C(6)-C(7)	1.324(6)	C(12)-C(13)-N(5)	115.5(3)
C(7)-N(3)	1.388(6)	C(10)-N(5)-C(13)	114.0(3)
C(7)-C(8)	1.486(5)	C(10)-N(5)-C(14)	123.6(3)
N(3)-C(5)	1.287(6)	C(13)-N(5)-C(14)	122.4(3)
C(8)-C(9)	1.493(5)	N(6)-C(14)-N(5)	119.2(3)
C(9)-N(4)	1.489(4)	N(6)-C(14)-S(3)	117.8(3)
N(4)-C(10)	1.242(4)	N(5)-C(14)-S(3)	122.9(2)
C(10)-N(5)	1.394(4)	C(14)-N(6)-C(15)	107.9(3)

C(10)-S(2)	1.769(4)	C(14)-S(3)-C(16)	87.28(17)
C(11)-C(12)	1.482(5)	C(16)-C(15)-N(6)	117.5(4)
C(12)-C(13)	1.327(5)	C(15)-C(16)-C(17)	128.8(4)
C(12)-S(2)	1.752(3)	C(15)-C(16)-S(3)	109.5(3)
C(13)-N(5)	1.405(5)	C(17)-C(16)-S(3)	121.7(3)
N(5)-C(14)	1.418(5)	N(1)-C(4)-S(1)	112.7(3)
C(14)-N(6)	1.272(5)	N(2)-C(4)-S(1)	122.6(4)
C(14)-S(3)	1.715(4)	C(4)-S(1)-C(2)	90.4(2)
N(6)-C(15)	1.379(5)	C(6)-N(2)-C(5)	105.0(4)
S(3)-C(16)	1.735(4)	C(6)-N(2)-C(4)	128.0(4)
C(15)-C(16)	1.320(5)	C(5)-N(2)-C(4)	127.0(4)
C(16)-C(17)	1.494(6)	C(7)-C(6)-N(2)	107.1(4)
C(3)-C(2)-C(1)	133.7(6)	C(6)-C(7)-N(3)	110.7(4)
C(3)-C(2)-S(1)	106.0(3)	C(6)-C(7)-C(8)	128.4(4)
C(1)-C(2)-S(1)	120.3(5)	N(3)-C(7)-C(8)	120.8(4)
C(2)-C(3)-N(1)	119.0(5)	C(5)-N(3)-C(7)	105.2(4)
C(3)-N(1)-C(4)	111.8(4)	N(3)-C(5)-N(2)	112.0(4)
N(1)-C(4)-N(2)	124.7(4)	C(7)-C(8)-C(9)	114.6(4)

Table 4 Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 106. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	116(6)	128(4)	99(3)	-9(3)	4(3)	-15(4)
C(2)	68(3)	93(3)	62(2)	12(2)	1(2)	1(2)
C(3)	52(2)	116(3)	99(3)	10(2)	10(2)	12(3)
N(1)	28(2)	94(2)	61(2)	9(2)	1(1)	20(2)
C(4)	47(2)	88(2)	57(2)	14(2)	-2(2)	7(2)
S(1)	40(1)	149(1)	100(1)	7(1)	-9(1)	1(1)
N(2)	47(2)	89(2)	61(2)	21(1)	2(2)	17(2)
C(6)	53(2)	86(2)	52(2)	21(2)	2(2)	13(2)
C(7)	48(2)	71(2)	62(2)	28(2)	1(2)	12(2)
N(3)	52(2)	114(3)	73(2)	18(2)	-4(2)	29(2)
C(5)	49(2)	120(3)	73(2)	21(2)	-7(2)	25(2)
C(8)	75(3)	63(2)	66(2)	19(2)	1(2)	21(2)
C(9)	61(3)	56(2)	60(2)	11(2)	-1(2)	25(2)
N(4)	45(2)	54(2)	54(2)	12(1)	0(2)	17(2)
C(10)	38(2)	45(2)	47(2)	9(1)	-3(2)	12(2)
C(11)	59(3)	60(2)	62(2)	19(2)	13(2)	19(2)
C(12)	45(2)	57(2)	51(2)	10(2)	-1(2)	12(2)
S(2)	44(1)	58(1)	53(1)	13(1)	7(1)	19(1)
C(13)	46(2)	57(2)	54(2)	21(2)	1(2)	12(2)
N(5)	41(2)	56(2)	52(2)	13(1)	3(1)	15(2)
C(14)	35(2)	52(2)	52(2)	8(1)	-6(2)	8(2)
N(6)	45(2)	59(2)	75(2)	19(2)	9(2)	14(2)
S(3)	41(1)	65(1)	56(1)	15(1)	3(1)	13(1)
C(15)	42(2)	73(2)	85(3)	12(2)	16(2)	21(2)
C(16)	37(2)	71(2)	58(2)	15(2)	6(2)	13(2)
C(17)	48(3)	88(3)	83(3)	11(2)	13(2)	18(2)

Table 5 Torsion angles [°] for 106.

C(1)-C(2)-C(3)-N(1)	-177.0(5)	C(13)-C(12)-S(2)-C(10)	-0.6(3)
S(1)-C(2)-C(3)-N(1)	2.8(6)	C(11)-C(12)-S(2)-C(10)	-178.4(3)
C(2)-C(3)-N(1)-C(4)	-4.7(7)	N(4)-C(10)-S(2)-C(12)	178.5(4)
C(3)-N(1)-C(4)-N(2)	-177.0(4)	N(5)-C(10)-S(2)-C(12)	-0.6(3)

C(3)-N(1)-C(4)-S(1)	4.3(5)	C(11)-C(12)-C(13)-N(5)	179.2(4)
N(1)-C(4)-S(1)-C(2)	-2.4(3)	S(2)-C(12)-C(13)-N(5)	1.6(4)
N(2)-C(4)-S(1)-C(2)	178.9(4)	N(4)-C(10)-N(5)-C(13)	-177.6(3)
C(3)-C(2)-S(1)-C(4)	-0.1(4)	S(2)-C(10)-N(5)-C(13)	1.6(4)
C(1)-C(2)-S(1)-C(4)	179.7(4)	N(4)-C(10)-N(5)-C(14)	4.8(5)
N(1)-C(4)-N(2)-C(6)	-6.3(7)	S(2)-C(10)-N(5)-C(14)	-176.0(2)
S(1)-C(4)-N(2)-C(6)	172.2(3)	C(12)-C(13)-N(5)-C(10)	-2.2(5)
N(1)-C(4)-N(2)-C(5)	171.0(4)	C(12)-C(13)-N(5)-C(14)	175.5(3)
S(1)-C(4)-N(2)-C(5)	-10.5(6)	C(10)-N(5)-C(14)-N(6)	177.5(3)
C(5)-N(2)-C(6)-C(7)	1.3(5)	C(13)-N(5)-C(14)-N(6)	0.1(5)
C(4)-N(2)-C(6)-C(7)	179.0(4)	C(10)-N(5)-C(14)-S(3)	-4.1(5)
N(2)-C(6)-C(7)-N(3)	-0.3(5)	C(13)-N(5)-C(14)-S(3)	178.5(3)
N(2)-C(6)-C(7)-C(8)	175.0(4)	N(5)-C(14)-N(6)-C(15)	-179.6(3)
C(6)-C(7)-N(3)-C(5)	-0.9(5)	S(3)-C(14)-N(6)-C(15)	1.9(4)
C(8)-C(7)-N(3)-C(5)	-176.6(3)	N(6)-C(14)-S(3)-C(16)	-1.5(3)
C(7)-N(3)-C(5)-N(2)	1.8(5)	N(5)-C(14)-S(3)-C(16)	-179.9(3)
C(6)-N(2)-C(5)-N(3)	-2.0(5)	C(14)-N(6)-C(15)-C(16)	-1.5(5)
C(4)-N(2)-C(5)-N(3)	-179.8(4)	N(6)-C(15)-C(16)-C(17)	179.0(4)
C(6)-C(7)-C(8)-C(9)	-102.5(5)	N(6)-C(15)-C(16)-S(3)	0.5(5)
N(3)-C(7)-C(8)-C(9)	72.3(5)	C(14)-S(3)-C(16)-C(15)	0.4(3)
C(7)-C(8)-C(9)-N(4)	66.9(5)	C(14)-S(3)-C(16)-C(17)	-178.2(4)
C(8)-C(9)-N(4)-C(10)	-173.0(4)		
C(9)-N(4)-C(10)-N(5)	-179.9(3)		
C(9)-N(4)-C(10)-S(2)	1.2(5)		

7-(5-Methyl-thiazol-2-yl)-9*H*-purin-6-ylamine 111 ($C_9H_8N_6S$)

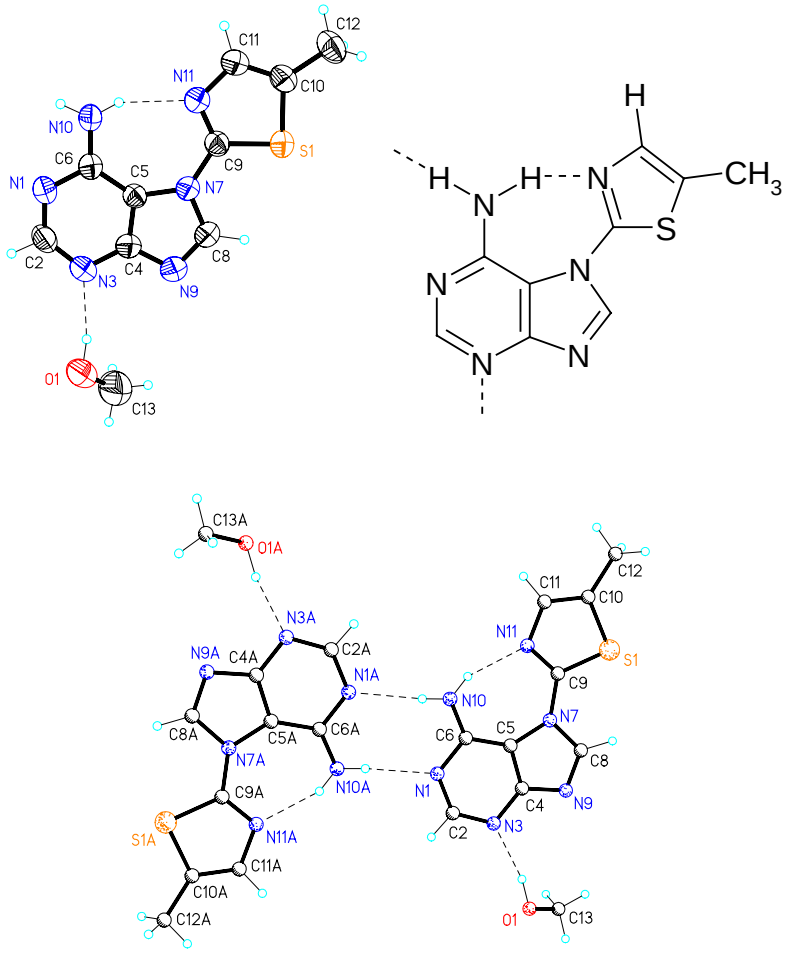


Table 1 Crystal data and structure refinement for 111.

Empirical formula	$C_{10}H_{12}N_6OS$
Formula weight	264.32
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/n
Unit cell dimensions	a = 7.332(8) Å b = 16.103(17) Å c = 10.241(10) Å β = 101.08(3)°
Volume	1187(2) $Å^3$
Z	4
Density (calculated)	1.480 Mg/m^3
Absorption coefficient	0.271 mm^{-1}
F(000)	552
Crystal size	0.6 x 0.5 x 0.3 mm^3
Theta range for data collection	2.39 to 26.72°.
Index ranges	-9<=h<=9, 0<=k<=20, 0<=l<=12
Reflections collected	13915
Independent reflections	2597 [R(int) = 0.0743]

Completeness to theta = 26.72°	98.9 %
Absorption correction	Empirical
Max. and min. transmission	0.99999 and 0.75832
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2494 / 0 / 200
Goodness-of-fit on F^2	1.038
Final R indices [I>2sigma(I)]	R1 = 0.0638, wR2 = 0.1499
R indices (all data)	R1 = 0.1101, wR2 = 0.1728
Largest diff. peak and hole	0.482 and -0.333 e.$Å^{-3}$

Table 2 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 111.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
N(1)	5239(4)	5864(2)	8814(3)	55(1)
N(3)	5222(4)	6989(2)	7314(3)	54(1)
N(7)	2911(4)	5399(2)	5347(3)	45(1)
N(9)	3678(4)	6717(2)	5081(3)	57(1)
N(10)	3799(6)	4631(2)	8269(4)	74(1)
N(11)	2292(4)	4008(2)	5750(3)	60(1)
S(1)	1156(1)	4408(1)	3340(1)	54(1)
C(2)	5656(5)	6623(2)	8474(4)	56(1)
C(4)	4289(4)	6485(2)	6375(3)	47(1)
C(5)	3837(4)	5678(2)	6588(3)	42(1)
C(6)	4275(5)	5361(2)	7892(3)	49(1)
C(8)	2892(5)	6063(2)	4511(4)	53(1)
C(9)	2210(4)	4611(2)	4950(3)	45(1)
C(10)	821(5)	3403(2)	3791(3)	52(1)
C(11)	1509(5)	3320(2)	5093(4)	61(1)
C(12)	-85(8)	2767(3)	2837(5)	70(1)
O(1)	5401(7)	8688(2)	6735(4)	127(2)
C(13)	5787(9)	8871(3)	5550(6)	114(2)
N(1)	5239(4)	5864(2)	8814(3)	55(1)

Table 3 Bond lengths [Å] and angles [°] for 111.

N(1)-C(2)	1.324(5)	C(9)-N(11)-C(11)	109.9(3)
N(1)-C(6)	1.338(4)	C(9)-S(1)-C(10)	88.98(16)
N(3)-C(2)	1.310(5)	N(3)-C(2)-N(1)	128.8(3)
N(3)-C(4)	1.341(4)	N(3)-C(2)-H(1)	115(2)
N(7)-C(8)	1.369(4)	N(1)-C(2)-H(1)	117(2)
N(7)-C(5)	1.395(4)	N(3)-C(4)-N(9)	123.9(3)
N(7)-C(9)	1.399(4)	N(3)-C(4)-C(5)	124.4(3)
N(9)-C(8)	1.286(5)	N(9)-C(4)-C(5)	111.7(3)
N(9)-C(4)	1.367(4)	C(4)-C(5)-N(7)	104.5(3)
N(10)-C(6)	1.306(5)	C(4)-C(5)-C(6)	118.5(3)
N(10)-H(4)	0.83(4)	N(7)-C(5)-C(6)	136.9(3)
N(10)-H(3)	0.83(4)	N(10)-C(6)-N(1)	118.1(3)
N(11)-C(9)	1.264(4)	N(10)-C(6)-C(5)	125.5(3)
N(11)-C(11)	1.364(5)	N(1)-C(6)-C(5)	116.3(3)
S(1)-C(9)	1.713(4)	N(9)-C(8)-N(7)	114.0(3)
S(1)-C(10)	1.713(4)	N(9)-C(8)-H(2)	125(2)
C(2)-H(1)	0.96(4)	N(7)-C(8)-H(2)	121(2)

C(4)-C(5)	1.370(4)	N(11)-C(9)-N(7)	122.6(3)
C(5)-C(6)	1.408(4)	N(11)-C(9)-S(1)	115.7(3)
C(8)-H(2)	0.99(4)	N(7)-C(9)-S(1)	121.7(2)
C(10)-C(11)	1.339(5)	C(11)-C(10)-C(12)	128.5(4)
C(10)-C(12)	1.482(5)	C(11)-C(10)-S(1)	108.5(3)
C(11)-H(5)	0.98(4)	C(12)-C(10)-S(1)	123.0(3)
C(12)-H(7)	0.88(5)	C(10)-C(11)-N(11)	116.9(3)
C(12)-H(8)	1.01(5)	C(10)-C(11)-H(5)	125(2)
C(12)-H(6)	1.00(6)	N(11)-C(11)-H(5)	118(2)
O(1)-C(13)	1.331(6)	C(10)-C(12)-H(7)	117(3)
O(1)-H(9)	0.97(7)	C(10)-C(12)-H(8)	107(3)
C(13)-H(13A)	0.9600	H(7)-C(12)-H(8)	107(4)
C(13)-H(13B)	0.9600	C(10)-C(12)-H(6)	114(3)
C(13)-H(13C)	0.9600	H(7)-C(12)-H(6)	108(4)
C(2)-N(1)-C(6)	119.4(3)	H(8)-C(12)-H(6)	103(4)
C(2)-N(3)-C(4)	112.4(3)	C(13)-O(1)-H(9)	116(3)
C(8)-N(7)-C(5)	105.2(3)	O(1)-C(13)-H(13A)	109.5
C(8)-N(7)-C(9)	124.6(3)	O(1)-C(13)-H(13B)	109.5
C(5)-N(7)-C(9)	130.1(3)	H(13A)-C(13)-H(13B)	109.5
C(8)-N(9)-C(4)	104.5(3)	O(1)-C(13)-H(13C)	109.5
C(6)-N(10)-H(4)	116(3)	H(13A)-C(13)-H(13C)	109.5
C(6)-N(10)-H(3)	119(3)	H(13B)-C(13)-H(13C)	109.5
H(4)-N(10)-H(3)	125(4)		

Table 4 Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 111. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1)	68(2)	52(2)	44(2)	-7(1)	2(1)	-8(1)
N(3)	60(2)	44(2)	55(2)	-7(1)	9(1)	-5(1)
N(7)	53(2)	41(2)	40(2)	0(1)	5(1)	2(1)
N(9)	70(2)	47(2)	51(2)	5(1)	8(1)	-2(1)
N(10)	116(3)	56(2)	39(2)	5(2)	-11(2)	-29(2)
N(11)	83(2)	48(2)	44(2)	2(1)	2(2)	-9(2)
S(1)	64(1)	53(1)	41(1)	-3(1)	1(1)	-1(1)
C(2)	62(2)	50(2)	53(2)	-14(2)	6(2)	-6(2)
C(4)	50(2)	42(2)	48(2)	1(1)	9(2)	2(1)
C(5)	45(2)	40(2)	41(2)	-4(1)	7(1)	1(1)
C(6)	58(2)	46(2)	40(2)	-3(2)	6(2)	0(2)
C(8)	63(2)	49(2)	45(2)	5(2)	4(2)	2(2)
C(9)	48(2)	43(2)	43(2)	-4(1)	7(2)	2(1)
C(10)	52(2)	48(2)	55(2)	-8(2)	11(2)	-2(2)
C(11)	80(3)	45(2)	54(2)	1(2)	6(2)	-8(2)
C(12)	80(3)	66(3)	63(3)	-22(2)	10(2)	-13(2)
O(1)	240(5)	55(2)	71(2)	-6(2)	-9(3)	-10(2)
C(13)	169(6)	90(4)	78(4)	-2(3)	16(4)	-9(4)

Table 5. Torsion angles [°] for 111.

C(4)-N(3)-C(2)-N(1)	-2.6(5)	C(4)-C(5)-C(6)-N(1)	-5.0(5)
C(6)-N(1)-C(2)-N(3)	1.4(6)	N(7)-C(5)-C(6)-N(1)	179.5(3)
C(2)-N(3)-C(4)-N(9)	-179.9(3)	C(4)-N(9)-C(8)-N(7)	0.7(4)
C(2)-N(3)-C(4)-C(5)	-0.2(5)	C(5)-N(7)-C(8)-N(9)	-0.4(4)

C(8)-N(9)-C(4)-N(3)	178.9(3)	C(9)-N(7)-C(8)-N(9)	-177.3(3)
C(8)-N(9)-C(4)-C(5)	-0.8(4)	C(11)-N(11)-C(9)-N(7)	-179.9(3)
N(3)-C(4)-C(5)-N(7)	-179.2(3)	C(11)-N(11)-C(9)-S(1)	0.9(4)
N(9)-C(4)-C(5)-N(7)	0.6(4)	C(8)-N(7)-C(9)-N(11)	178.4(3)
N(3)-C(4)-C(5)-C(6)	4.0(5)	C(5)-N(7)-C(9)-N(11)	2.3(5)
N(9)-C(4)-C(5)-C(6)	-176.3(3)	C(8)-N(7)-C(9)-S(1)	-2.4(5)
C(8)-N(7)-C(5)-C(4)	-0.1(3)	C(5)-N(7)-C(9)-S(1)	-178.5(2)
C(9)-N(7)-C(5)-C(4)	176.6(3)	C(10)-S(1)-C(9)-N(11)	-0.9(3)
C(8)-N(7)-C(5)-C(6)	175.9(4)	C(10)-S(1)-C(9)-N(7)	179.9(3)
C(9)-N(7)-C(5)-C(6)	-7.5(6)	C(9)-S(1)-C(10)-C(11)	0.5(3)
C(2)-N(1)-C(6)-N(10)	-176.5(4)	C(9)-S(1)-C(10)-C(12)	-179.2(4)
C(2)-N(1)-C(6)-C(5)	2.6(5)	C(12)-C(10)-C(11)-N(11)	179.5(4)
C(4)-C(5)-C(6)-N(10)	174.0(4)	S(1)-C(10)-C(11)-N(11)	-0.2(4)
N(7)-C(5)-C(6)-N(10)	-1.6(6)	C(9)-N(11)-C(11)-C(10)	-0.4(5)

Additional Information

Nr	Type	Donor --- H....Acceptor	D - H	H...A	D...A	D - H...A
1	Intra	N(10) -- H(3) .. N(11)	0.83(4)	2.05(4)	2.790(6)	149(3)
2		N(10) -- H(4) .. N(1)	0.83(4)	2.21(4)	3.041(6)	173(3)
3		O(1) -- H(9) .. N(3)	0.97(6)	1.86(6)	2.808(5)	163(6)

5-Azidomethyl-thiazol-2-ylamine 115 ($C_4H_5N_5S$)

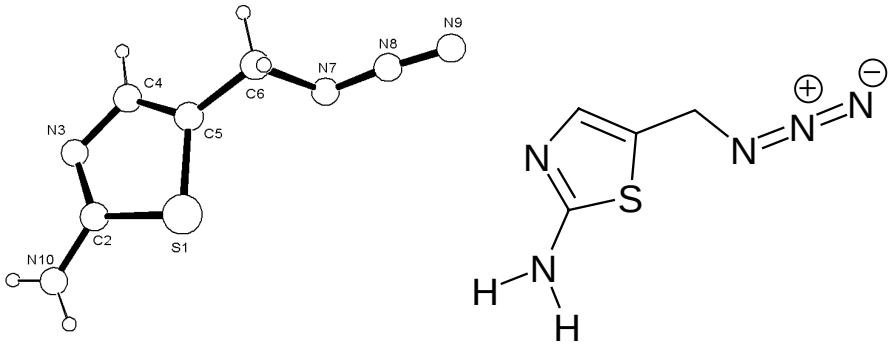


Table 1 Crystal data and structure refinement for 115.

Empirical formula	$C_4H_5N_5S$
Formula weight	155.19
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/c
Unit cell dimensions	a = 12.911(3) Å b = 5.4386(10) Å c = 10.732(2) Å β= 113.164(3)°
Volume	692.8(2) $Å^3$
Z	4
Density (calculated)	1.488 Mg/m^3
Absorption coefficient	0.392 mm^{-1}
F(000)	320
Crystal size	0.4 x 0.1 x 0.05 mm^3
Theta range for data collection	1.72 to 26.45°.
Index ranges	-16<=h<=16, -6<=k<=6, -13<=l<=13
Reflections collected	4200
Independent reflections	1364 [R(int) = 0.0476]
Completeness to theta = 26.45°	95.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1 and 0.1731051
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1364 / 70 / 92
Goodness-of-fit on F^2	1.094
Final R indices [I>2sigma(I)]	R1 = 0.0561, wR2 = 0.1104
R indices (all data)	R1 = 0.0965, wR2 = 0.1271
Extinction coefficient	0.016(4)
Largest diff. peak and hole	0.209 and -0.222 e.$Å^{-3}$

Table 2 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 115.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)

S(1)	7343(1)	11291(2)	1816(1)	56(1)
C(2)	8588(3)	10938(6)	3245(3)	48(1)
N(3)	9171(2)	8985(5)	3227(2)	51(1)
C(4)	8636(3)	7705(6)	2037(3)	52(1)
C(5)	7661(3)	8603(6)	1162(3)	49(1)
C(6)	6880(3)	7504(7)	-138(3)	62(1)
N(7)	6802(3)	9108(6)	-1288(3)	65(1)
N(8)	5971(3)	8740(5)	-2333(3)	58(1)
N(9)	5241(3)	8569(6)	-3350(3)	78(1)
N(10)	8900(3)	12563(5)	4267(3)	71(1)

Table 3 Bond lengths [Å] and angles [°] for 115.

S(1)-C(5)	1.740(3)	N(3)-C(2)-N(10)	123.9(3)
S(1)-C(2)	1.742(3)	N(3)-C(2)-S(1)	114.5(2)
C(2)-N(3)	1.306(4)	N(10)-C(2)-S(1)	121.6(3)
C(2)-N(10)	1.341(4)	C(2)-N(3)-C(4)	110.0(3)
N(3)-C(4)	1.378(4)	C(5)-C(4)-N(3)	117.3(3)
C(4)-C(5)	1.332(4)	C(4)-C(5)-C(6)	128.2(3)
C(5)-C(6)	1.488(4)	C(4)-C(5)-S(1)	109.3(2)
C(6)-N(7)	1.482(4)	C(6)-C(5)-S(1)	122.4(3)
N(7)-N(8)	1.226(4)	N(7)-C(6)-C(5)	110.1(3)
N(8)-N(9)	1.131(4)	N(8)-N(7)-C(6)	114.5(3)
C(5)-S(1)-C(2)	88.84(16)	N(9)-N(8)-N(7)	173.6(4)

Table 4 Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 115. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	61(1)	53(1)	44(1)	-2(1)	10(1)	7(1)
C(2)	57(2)	44(2)	41(2)	0(2)	16(2)	1(2)
N(3)	55(2)	45(2)	45(1)	-5(1)	12(1)	1(1)
C(4)	64(2)	43(2)	48(2)	-5(2)	21(2)	2(2)
C(5)	63(2)	44(2)	39(2)	-3(2)	19(2)	-5(2)
C(6)	83(2)	58(2)	40(2)	-1(2)	19(2)	-14(2)
N(7)	72(2)	76(2)	39(2)	6(2)	14(1)	-13(2)
N(8)	68(2)	60(2)	46(2)	6(2)	21(2)	5(2)
N(9)	75(2)	97(3)	52(2)	10(2)	13(2)	10(2)
N(10)	78(2)	57(2)	53(2)	-16(2)	2(2)	19(2)

Table 5 Torsion angles [°] for 115.

C(5)-S(1)-C(2)-N(3)	-0.5(3)
C(5)-S(1)-C(2)-N(10)	179.7(3)
N(10)-C(2)-N(3)-C(4)	-179.4(3)
S(1)-C(2)-N(3)-C(4)	0.9(4)
C(2)-N(3)-C(4)-C(5)	-0.9(4)
N(3)-C(4)-C(5)-C(6)	-175.4(3)
N(3)-C(4)-C(5)-S(1)	0.5(4)
C(2)-S(1)-C(5)-C(4)	0.0(3)
C(2)-S(1)-C(5)-C(6)	176.2(3)
C(4)-C(5)-C(6)-N(7)	-116.2(4)
S(1)-C(5)-C(6)-N(7)	68.4(4)
C(5)-C(6)-N(7)-N(8)	-160.9(3)
C(6)-N(7)-N(8)-N(9)	-180(100)

5-Piperidin-1-ylmethyl-3*H*-thiazol-2-one 134b ($C_9H_{14}N_2OS$)

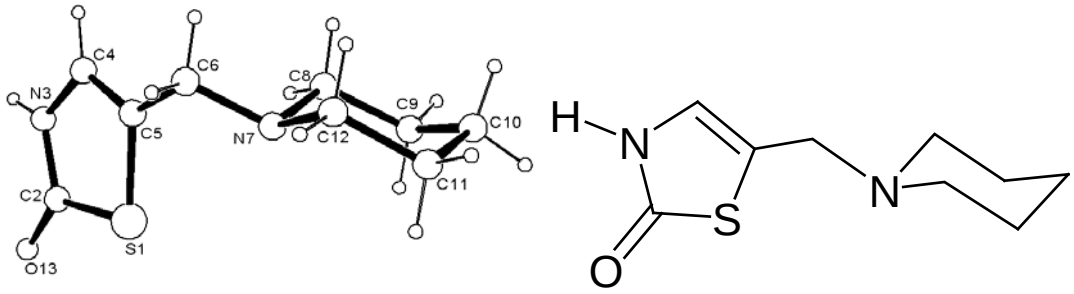


Table 1 Crystal data and structure refinement for 134b.

Empirical formula	$C_9H_{14}N_2OS$
Formula weight	198.28
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/c
Unit cell dimensions	a = 15.9889(13) Å b = 5.4534(4) Å c = 12.6917(10) Å β= 107.9390(10)°
Volume	1052.84(14) $Å^3$
Z	4
Density (calculated)	1.251 Mg/m^3
Absorption coefficient	0.272 mm^{-1}
F(000)	424
Crystal size	0.4 x 0.2 x 0.05 mm^3
Theta range for data collection	2.68 to 26.42°.
Index ranges	-20<=h<=19, -6<=k<=6, -15<=l<=15
Reflections collected	9271
Independent reflections	2138 [R(int) = 0.0423]
Completeness to theta = 26.42°	99.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1 and 0.364525
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2138 / 216 / 165
Goodness-of-fit on F^2	1.067
Final R indices [I>2sigma(I)]	R1 = 0.0473, wR2 = 0.1075
R indices (all data)	R1 = 0.0780, wR2 = 0.1257
Extinction coefficient	0.016(3)
Largest diff. peak and hole	0.258 and -0.241 e.$Å^{-3}$

Table 2 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 134b.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
S(1)	3417(1)	3571(1)	7214(1)	51(1)
C(2)	4124(2)	4003(4)	8568(2)	47(1)

N(3)	4493(1)	6239(3)	8637(1)	43(1)
C(4)	4261(2)	7565(4)	7659(2)	43(1)
C(5)	3706(2)	6420(4)	6807(2)	42(1)
C(6)	3378(2)	7152(5)	5613(2)	51(1)
N(7)	2461(1)	6536(4)	5119(2)	53(1)
O(13)	4257(1)	2486(3)	9326(1)	62(1)
C(8)	1932(10)	8400(40)	5568(15)	70(2)
C(9)	962(8)	7860(30)	5157(10)	83(2)
C(10)	603(8)	7760(30)	3930(11)	84(2)
C(11)	1145(10)	6070(30)	3442(10)	81(2)
C(12)	2114(9)	6770(40)	3901(15)	71(2)
C(8')	1863(8)	7910(30)	5471(13)	73(2)
C(9')	953(7)	6830(30)	5010(8)	83(2)
C(10')	690(7)	6860(30)	3743(9)	86(2)
C(11')	1379(7)	5420(30)	3402(8)	74(2)
C(12')	2291(7)	6420(30)	3927(12)	67(2)

Table 3 Bond lengths [Å] and angles [°] for 134b.

S(1)-C(5)	1.744(2)	C(5)-C(4)-N(3)	114.4(2)
S(1)-C(2)	1.758(2)	C(4)-C(5)-C(6)	129.7(2)
C(2)-O(13)	1.237(3)	C(4)-C(5)-S(1)	110.46(17)
C(2)-N(3)	1.346(3)	C(6)-C(5)-S(1)	119.70(17)
N(3)-C(4)	1.385(3)	N(7)-C(6)-C(5)	111.7(2)
C(4)-C(5)	1.326(3)	C(8')-N(7)-C(6)	116.2(5)
C(5)-C(6)	1.497(3)	C(8')-N(7)-C(12')	115.6(8)
C(6)-N(7)	1.446(3)	C(6)-N(7)-C(12')	107.5(5)
N(7)-C(8')	1.391(15)	C(8')-N(7)-C(12)	102.5(10)
N(7)-C(12')	1.454(15)	C(6)-N(7)-C(12)	115.9(7)
N(7)-C(12)	1.478(18)	C(12')-N(7)-C(12)	13.1(10)
N(7)-C(8)	1.538(17)	C(8')-N(7)-C(8)	10.3(11)
C(8)-C(9)	1.505(11)	C(6)-N(7)-C(8)	106.6(6)
C(9)-C(10)	1.485(10)	C(12')-N(7)-C(8)	117.8(10)
C(10)-C(11)	1.521(10)	C(12)-N(7)-C(8)	105.0(10)
C(11)-C(12)	1.526(10)	C(9)-C(8)-N(7)	111.6(10)
C(8')-C(9')	1.510(9)	C(10)-C(9)-C(8)	113.3(10)
C(9')-C(10')	1.531(9)	C(9)-C(10)-C(11)	111.4(8)
C(10')-C(11')	1.518(8)	C(10)-C(11)-C(12)	109.4(8)
C(11')-C(12')	1.506(9)	N(7)-C(12)-C(11)	112.8(12)
C(5)-S(1)-C(2)	91.22(11)	N(7)-C(8')-C(9')	110.0(9)
O(13)-C(2)-N(3)	126.0(2)	C(8')-C(9')-C(10')	108.8(8)
O(13)-C(2)-S(1)	125.17(19)	C(11')-C(10')-C(9')	107.8(6)
N(3)-C(2)-S(1)	108.83(17)	C(12')-C(11')-C(10')	112.1(7)
C(2)-N(3)-C(4)	115.01(19)	N(7)-C(12')-C(11')	108.7(9)

Table 4 Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 134b. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	57(1)	47(1)	42(1)	1(1)	2(1)	-7(1)
C(2)	49(1)	47(1)	40(1)	0(1)	8(1)	-4(1)
N(3)	48(1)	41(1)	34(1)	-1(1)	5(1)	-3(1)
C(4)	47(1)	39(1)	43(1)	3(1)	12(1)	2(1)
C(5)	42(1)	43(1)	39(1)	3(1)	9(1)	6(1)
C(6)	50(1)	60(2)	40(1)	6(1)	8(1)	2(1)
N(7)	52(1)	66(1)	36(1)	3(1)	6(1)	2(1)

O(13)	77(1)	53(1)	44(1)	9(1)	2(1)	-13(1)
C(8)	56(3)	86(6)	58(4)	-10(4)	4(3)	15(3)
C(9)	57(3)	110(6)	71(4)	-17(4)	3(3)	14(4)
C(10)	58(3)	113(6)	69(4)	-5(4)	2(3)	11(4)
C(11)	58(5)	116(6)	56(3)	-13(4)	-3(3)	8(4)
C(12)	59(4)	107(5)	39(2)	2(3)	4(3)	6(4)
C(8')	57(3)	94(6)	57(3)	-8(3)	1(3)	16(3)
C(9')	54(2)	119(6)	70(3)	-16(4)	11(3)	11(4)
C(10')	54(3)	122(6)	66(3)	-11(4)	-4(3)	13(4)
C(11')	55(4)	112(5)	48(2)	-3(3)	4(3)	-1(4)
C(12')	53(3)	99(5)	39(2)	3(3)	-1(3)	3(4)

Table 5 Torsion angles [°] for 134b.

C(5)-S(1)-C(2)-O(13)	-177.4(2)
C(5)-S(1)-C(2)-N(3)	2.45(18)
O(13)-C(2)-N(3)-C(4)	177.8(2)
S(1)-C(2)-N(3)-C(4)	-2.1(2)
C(2)-N(3)-C(4)-C(5)	0.3(3)
N(3)-C(4)-C(5)-C(6)	-173.5(2)
N(3)-C(4)-C(5)-S(1)	1.6(3)
C(2)-S(1)-C(5)-C(4)	-2.33(18)
C(2)-S(1)-C(5)-C(6)	173.4(2)
C(4)-C(5)-C(6)-N(7)	-141.9(3)
S(1)-C(5)-C(6)-N(7)	43.3(3)
C(5)-C(6)-N(7)-C(8')	70.1(10)
C(5)-C(6)-N(7)-C(12')	-158.7(8)
C(5)-C(6)-N(7)-C(12)	-169.5(9)
C(5)-C(6)-N(7)-C(8)	74.1(9)
C(8')-N(7)-C(8)-C(9)	-18(7)
C(6)-N(7)-C(8)-C(9)	-177.0(10)
C(12')-N(7)-C(8)-C(9)	62.3(16)
C(12)-N(7)-C(8)-C(9)	59.5(16)
N(7)-C(8)-C(9)-C(10)	-55.9(16)
C(8)-C(9)-C(10)-C(11)	50.8(14)
C(9)-C(10)-C(11)-C(12)	-51.2(14)
C(8')-N(7)-C(12)-C(11)	-52.9(14)
C(6)-N(7)-C(12)-C(11)	179.5(8)
C(12')-N(7)-C(12)-C(11)	128(7)
C(8)-N(7)-C(12)-C(11)	-63.1(14)
C(10)-C(11)-C(12)-N(7)	60.8(15)
C(6)-N(7)-C(8')-C(9')	-172.1(7)
C(12')-N(7)-C(8')-C(9')	60.6(15)
C(12)-N(7)-C(8')-C(9')	60.5(14)
C(8)-N(7)-C(8')-C(9')	166(9)
N(7)-C(8')-C(9')-C(10')	-59.7(13)
C(8')-C(9')-C(10')-C(11')	57.4(10)
C(9')-C(10')-C(11')-C(12')	-56.2(11)
C(8')-N(7)-C(12')-C(11')	-56.6(13)
C(6)-N(7)-C(12')-C(11')	171.8(7)
C(12)-N(7)-C(12')-C(11')	-56(6)
C(8)-N(7)-C(12')-C(11')	-67.9(13)
C(10')-C(11')-C(12')-N(7)	53.6(12)

Selbständigkeitserklärung

Hiermit erkläre ich, daß ich die vorliegende Arbeit selbständig und nur unter Verwendung der angegebenen Literatur und Hilfsmittel angefertigt habe.

Chemnitz, den 15.06.2005

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Curriculum Vitae

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1983–1989	Al-Shamella School for boys
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Awards	
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Publications and Poster Exhibitions

- "Rearrangement Reactions; 14: Synthesis of Functionalized Thiazoles via Attack of Heteroatom Nucleophiles on Allenyl Isothiocyantes" Klaus Banert, **Baker Jawabrah Al-Hourani**, Stefan Groth, Kai Vrobel *(In Printing, Synthesis)*
- Contribution to GDCh conference (ORCHEM 2004, 9^{th} – 11^{th} of Sep. 04 in Bad Nauheim in Germany). Poster title is "[3,3] Sigmatropic Rearrangement and Succeeding Reactions of Substituted Thiocyanates and an Enynyl Isothiocyanate"
- J. R. Al Dulayymi, M. S. Baird, H. H. Hussain, **B. J. Alhourani**, A.-M. Y. Alhabashna, S. J. Coles, M. B. Hursthouse, *Tetrahedron Letters* **2000**, *41*, 4205–4208.